



STANDARD COMMERCIAL DRUG FORMULARY  
PRIOR AUTHORIZATION GUIDELINES

OMBITASVIR/PARITAPREVIR/RITONAVIR

Generic	Brand	HICL	GCN	Exception/Other
OMBITASVIR/PARITAPREVIR/ RITONAVIR	TECHNIVIE	41734		

**\*\*\*\*\*Customer Service/PAC Alert\*\*\*\*\***  
**(For Internal Use Only)**

**THIS IS A HIGH-IMPACT MEDICATION. DO NOT OVERRIDE OR APPROVE WITHOUT  
SUBMITTING FOR PHARMACIST REVIEW.**

**GUIDELINES FOR USE**

- Does the patient meet **ALL** of the following criteria?
  - Age at least 18 years old
  - Diagnosis of hepatitis C, genotype 4
  - Patient is treatment naïve or treatment experienced (previous treatment with peginterferon/ribavirin)
  - Currently supervised by a gastroenterologist, infectious disease specialist, physician specializing in the treatment of hepatitis (for example, a hepatologist), or a specially trained group such as ECHO (Extension for Community Healthcare Outcomes) model

If yes, continue to #2.

If no, do not approve.

**DENIAL TEXT:** See the denial text at the end of the guideline.

**CONTINUED ON NEXT PAGE**



STANDARD COMMERCIAL DRUG FORMULARY  
PRIOR AUTHORIZATION GUIDELINES

OMBITASVIR/PARITAPREVIR/RITONAVIR

**GUIDELINES FOR USE (CONTINUED)**

2. Does the patient have one or more of the following conditions?

- Patient is on hemodialysis
- Moderate or severe liver impairment (Child-Pugh B or Child-Pugh C), or decompensated liver disease
- A limited life expectancy (less than 12 months) due to non-liver related comorbid conditions (e.g., physician attestation)
- Concurrent use with any of these medications (contraindicated or not recommended by the manufacturer): alfuzosin, carbamazepine, phenytoin, phenobarbital, rifampin, ergotamine, dihydroergotamine, ergonovine, methylegonovine, ethinyl estradiol containing medications (such as combined oral contraceptives, NuvaRing, Ortho Evra or Xulane transdermal patch system), lovastatin, simvastatin, pimozide, efavirenz (Atripla, Sustiva), Revatio (sildenafil dose of 20mg and/or dosed TID for PAH), triazolam, oral midazolam, lopinavir/ritonavir, rilpivirine, salmeterol
- Prior use (failure of a full course of therapy) or concurrent use of any HCV protease inhibitors including Olysio (simeprevir), Victrelis (boceprevir), or Incivek (telaprevir)
- Prior use (failure of a full course of therapy) or concurrent use of any NS5B polymerase inhibitor including Sovaldi (sofosbuvir)
- Prior use (failure of a full course of therapy) of concurrent use of any NS5B polymerase inhibitor/NS5A inhibitor including Harvoni (ledipasvir/sofosbuvir)
- Prior use (short trial or failure of a full course of therapy) of Viekira Pak or Viekira XR

If yes, do not approve.

**DENIAL TEXT:** See the denial text at the end of the guideline.

If no, continue to #3.

3. Does the patient have evidence of current HCV infection and chronic HCV infection as documented by one detectable HCV RNA level within the past 6 months?

If yes, continue to #4.

If no, do not approve.

**DENIAL TEXT:** See the denial text at the end of the guideline.

**CONTINUED ON NEXT PAGE**



STANDARD COMMERCIAL DRUG FORMULARY  
PRIOR AUTHORIZATION GUIDELINES

OMBITASVIR/PARITAPREVIR/RITONAVIR

**GUIDELINES FOR USE (CONTINUED)**

4. Does the patient meet **ONE** of the following criteria?

- Patient has a contraindication to therapy with Epclusa, Harvoni, **AND** Mavyret
- Patient has previously failed a short trial with Epclusa, Harvoni or Mavyret (e.g., adverse effect early in therapy); [**NOTE:** An individual who has completed a full course of therapy with Epclusa, Harvoni or Mavyret that did not achieve SVR will not be approved.]

If yes, continue to #5.

If no, do not approve.

**DENIAL TEXT:** See the denial text at the end of the guideline.

5. Is the requested medication being used with ribavirin?

If yes, **approve for 12 weeks by HICL for #56 tablets (1 monthly carton) per 28 days.**

(**NOTE:** Approval allows patients to complete a total maximum of 12 weeks of therapy.)

If no, continue to #6.

6. Is the patient treatment naïve and without cirrhosis?

If yes, continue to #7.

If no, do not approve.

**DENIAL TEXT:** See the denial text at the end of the guideline.

7. Does the patient have an intolerance or contraindication to ribavirin?

If yes, **approve for 12 weeks by HICL for #56 tablets (1 monthly carton) per 28 days.**

(**NOTE:** Approval allows patients to complete a total maximum of 12 weeks of therapy.)

If no, do not approve.

**DENIAL TEXT:** See the denial text at the end of the guideline.

**CONTINUED ON NEXT PAGE**



STANDARD COMMERCIAL DRUG FORMULARY  
PRIOR AUTHORIZATION GUIDELINES

OMBITASVIR/PARITAPREVIR/RITONAVIR

**GUIDELINES FOR USE (CONTINUED)**

**DENIAL TEXT:** The guideline named **OMBITASVIR/PARITAPREVIR/RITONAVIR (Technivie)** requires a diagnosis of chronic hepatitis C, genotype 4 without cirrhosis or with compensated cirrhosis (Child-Pugh A). The following criteria must also be met:

- Patient is treatment naïve or treatment experienced (previous treatment with peginterferon/ribavirin)
- Concurrent use with ribavirin unless patient is treatment naïve without cirrhosis and has an intolerance or contraindication to ribavirin
- Patient is at least 18 years old
- Patient has failed a previous trial of Harvoni or Epclusa or Mavyret (intolerance, adverse effect or contraindication to all three therapies) (**NOTE:** An individual who has completed a full course of therapy with Harvoni, Epclusa or Mavyret that did not achieve SVR will not be approved)
- Currently supervised by a gastroenterologist, infectious disease specialist, physician specializing in the treatment of hepatitis (for example, a hepatologist), or a specially trained group such as ECHO (Extension for Community Healthcare Outcomes) model
- Evidence of current HCV infection and chronic HCV infection as documented by at least one detectable HCV RNA levels within past 6 months

A total of 12 weeks of therapy will be approved.

**Technivie will not be approved for the following patients:**

- Patient using any of the following medications concurrently while on Technivie: alfuzosin, carbamazepine, phenytoin, phenobarbital, rifampin, ergotamine, dihydroergotamine, ergonovine, methylergonovine, ethinyl estradiol containing medications (such as combined oral contraceptives, NuvaRing, Ortho Evra or Xulane transdermal patch system), lovastatin, simvastatin, pimozide, efavirenz, Revatio, triazolam, oral midazolam, lopinavir/ritonavir, rilpivirine, or salmeterol
- Patients with moderate or severe liver impairment (Child Pugh B or Child Pugh C)
- Patient is on hemodialysis
- Individual with a limited life expectancy (less than 12 months) due to non-liver related comorbid conditions
- Any patient with prior use of or concurrent use of Viekira Pak or Viekira XR, or a previous failure of any of the following regimens: a nucleotide NS5B polymerase inhibitor including Sovaldi (sofosbuvir), a combination NS5B polymerase inhibitor/NS5A inhibitor including Harvoni (ledipasvir/sofosbuvir), and/or a HCV protease inhibitor including Olysio (simeprevir), Victrelis (boceprevir), and Incivek (telaprevir)

**CONTINUED ON NEXT PAGE**



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PRIOR AUTHORIZATION GUIDELINES

OMBITASVIR/PARITAPREVIR/RITONAVIR

**RATIONALE**

Ensure appropriate utilization of Technivie (ombitasvir/paritaprevir/ritonavir) based on FDA approved indication, current treatment guideline recommendations and other P&T approved criteria to promote cost-effective use.

**FDA APPROVED INDICATIONS**

For the treatment of chronic hepatitis C genotype 4 infection in adults without cirrhosis or with compensated cirrhosis, for use in combination with ribavirin.

TECHNIVIE administered without ribavirin for 12 weeks may be considered for treatment-naïve patients without cirrhosis who cannot take or tolerate ribavirin.

TECHNIVIE includes ombitasvir, a hepatitis C virus NS5A inhibitor, and paritaprevir, a hepatitis C virus NS3/4A protease inhibitor with ritonavir, a CYP3A inhibitor.

The efficacy of TECHNIVIE has not been studied in subjects who have failed prior treatment with another NS5A inhibitor, NS3/4A protease inhibitor, or NS5B inhibitor.

**FDA APPROVED DOSAGE**

Recommended dosage: Two ombitasvir, paritaprevir, ritonavir 12.5/75/50 mg tablets once daily (in the morning) with a meal without regard to fat or calorie content. Take with ribavirin.

**OTHER INFORMATION**

**AASLD/IDSA Guidance - Initial Treatment of Patients Initiating Therapy for HCV infection – For Genotype 4 Infection [From July 2016 Guideline update; see [hcvguidelines.org](http://hcvguidelines.org) for most recent recommendations]**

Genotype	Recommended Regimen
<b>4</b>	4. Epclusa for 12 weeks for treatment naïve patients with genotype 4 (for patients with or without cirrhosis) - <b>Rating 1A</b> 5. Technivie and ribavirin for 12 weeks, for treatment naïve patients (for patients with or without cirrhosis) - <b>Rating 1A</b> 6. Zepatier daily for 12 weeks (for patients with or without cirrhosis) - - <b>Rating IIa-B</b> 7. Harvoni daily for 12 weeks, for treatment naïve patients with genotype 4 (for patients with or without cirrhosis) - <b>Rating IIa-B</b>

CONTINUED ON NEXT PAGE



STANDARD COMMERCIAL DRUG FORMULARY  
PRIOR AUTHORIZATION GUIDELINES

OMBITASVIR/PARITAPRE VIR/RITONAVIR

FDA APPROVED INDICATIONS (CONTINUED)

OTHER INFORMATION

AASLD/IDSA Guidance - Retreatment of HCV infection (recommendations for patients in whom previous treatment has failed) [From July 2016 Guideline update; see [hcvguidelines.org](http://hcvguidelines.org) for most recent recommendations]

GT	Previous agent/regimen failed	Recommended Regimen
4	Peginterferon/ribavirin regimen	<ol style="list-style-type: none"><li>5. Eplclusa for 12 weeks - <b>Rating 1A</b></li><li>6. Technivie with ribavirin for 12 weeks - <b>Rating 1A</b></li><li>7. Zepatier daily for 12 weeks (use 16 weeks if previous on-treatment virologic failure after peg/RBV, add ribavirin for if previous failure to suppress or patient had breakthrough) - <b>Rating IIa-B</b></li><li>8. Harvoni daily for 12 weeks (add ribavirin if cirrhosis and patient is eligible for ribavirin), <i>Alternative</i>, if cirrhosis, is Harvoni for 24 weeks - <b>Rating IIa-B</b></li></ol>

EFFICACY

The approval of Technivie is based on data from the PEARL-I study, which was a randomized, global, multicenter, open-label trial that consisted of 135 adults with HCV genotype 4 infection without cirrhosis. The participants were either treatment-naïve (64%) or did not achieve a virologic response with prior treatment with pegylated interferon/ribavirin (pegIFN/RBV) (36%). Those with previous exposure to HCV direct-acting antivirals were excluded. Participants were randomized (1:1 ratio) to receive ombitasvir 25mg, paritaprevir 150mg, and ritonavir 100mg once daily with or without ribavirin for 12 weeks. The ribavirin dosage was 1000mg per day for subjects weighing less than 75kg or 1200mg per day for subjects weighing greater than or equal to 75kg. The primary endpoint was sustained virologic response defined as HCV RNA below the lower limit of quantification (<LLOQ) 12 weeks after the end of treatment (SVR12) using the COBAS TaqMan HCV test (version 2.0), for use with the High Pure System, which has an LLOQ of 25 IU per mL.

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STANDARD COMMERCIAL DRUG FORMULARY  
PRIOR AUTHORIZATION GUIDELINES

OMBITASVIR/PARITAPREVR/RITONAVIR

FDA APPROVED INDICATIONS (CONTINUED)

EFFICACY

Table 1. SVR12 for HCV Genotype 4-infected Subjects without Cirrhosis (from *Technivie Prescribing Information*)

Treatment outcome	Ombitasvir + Paritaprevir + Ritonavir with RBV for 12 weeks		Ombitasvir + Paritaprevir + Ritonavir for 12 weeks
	Treatment-naïve	Treatment- experienced	Treatment-naïve
	% (n/N)	% (n/N)	% (n/N)
<b>Overall SVR12</b>	100 % (42/42)	100% (49/49)	91% (40/44)
<b>Outcome for subjects without SVR12</b>			
On-treatment VF <sup>a</sup>	0% (0/42)	0% (0/49)	2% (1/44)
Relapse <sup>b</sup>	0% (0/42)	0% (0/49)	5% (2/42)
Other <sup>c</sup>	0% (0/42)	0% (0/49)	2% (1/44)

VF = virologic failure

a. On-treatment VF was defined as confirmed HCV  $\geq 25$  IU/mL after HCV RNA  $< 25$  IU/mL during treatment, confirmed increase from nadir in HCV RNA  $> 1 \log_{10}$  IU/mL during treatment, or HCV RNA  $\geq 25$  IU/mL persistently during treatment with at least 6 weeks of treatment.

b. Relapse was defined as confirmed HCV RNA  $\geq 25$  IU/mL post-treatment before or during SVR12 window among subjects with HCV RNA less than 25 IU/mL at last observation during at least 11 weeks of treatment.

c. Other includes subjects not achieving SVR12 but not experiencing on-treatment VF or relapse (e.g. lost to follow-up).

CONTINUED ON NEXT PAGE





**STANDARD COMMERCIAL DRUG FORMULARY  
PRIOR AUTHORIZATION GUIDELINES**

**OMBITASVIR/PARITAPRE VIR/RITONAVIR**

**FDA APPROVED INDICATIONS (CONTINUED)**

**SAFETY**

Technivie is contraindicated in patients with severe hepatic impairment and those with known hypersensitivity to ritonavir (e.g. toxic epidermal necrolysis, Stevens-Johnson syndrome). Co-administration of Technivie is also contraindicated with drugs that are highly dependent on CYP3A for clearance as well as moderate and strong inducers of CYP3A. Since Technivie is to be used in combination with ribavirin, the contraindications to ribavirin also apply e.g., pregnancy, autoimmune hepatitis, hemoglobinopathies, creatinine clearance less than 50 mL/min, coadministration with didanosine, known hypersensitivity reactions such as Stevens-Johnson syndrome, toxic, epidermal necrolysis, and erythema multiforme to ribavirin).

Technivie has warnings and precautions in place regarding ALT elevations, drug interactions, and the risks associated with ribavirin combination treatment.

Technivie may affect the plasma concentrations of other drugs since paritaprevir is an inhibitor of OATP1B1 and OATP1B3, paritaprevir and ritonavir are inhibitors of BCRP and P-glycoprotein (P-gp), and ritonavir is an inhibitor of CYP3A4. Co-administration of Technivie with drugs that are substrates of CYP3A, P-gp, BCRP, OATP1B1 or OATP1B3 may result in increased plasma concentrations of such drugs.

Other drugs may also affect the plasma concentrations of Technivie. Since paritaprevir and ritonavir are primarily metabolized by CYP3A enzymes, co-administration of Technivie with strong inhibitors of CYP3A may increase paritaprevir and ritonavir concentrations. Ombitasvir, paritaprevir and ritonavir are substrates of P-gp whereas paritaprevir is a substrate of BCRP, OATP1B1 and OATP1B3. Drugs which inhibit P-gp, BCRP, OATP1B1 or OATP1B3 may increase the plasma concentrations of the various components of Technivie.

Established drug interactions include certain antiarrhythmics, anti-fungals, antipsychotics, calcium channel blockers, corticosteroids, diuretics, HIV anti-viral agents, statins, immunosuppressants, long-acting beta-adrenoceptor agonist, narcotic analgesics, proton pump inhibitors, sedatives/hypnotics.

The most common adverse drug reactions (ADRs) were asthenia, fatigue, nausea and insomnia. The incidence of these ADRs is shown in Table 2.

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STANDARD COMMERCIAL DRUG FORMULARY  
PRIOR AUTHORIZATION GUIDELINES

OMBITASVIR/PARITAPREVR/RITONAVIR

FDA APPROVED INDICATIONS (CONTINUED)

SAFETY

Table 2. Selected Adverse Reactions (all Grades) with  $\geq 5\%$  Frequency Reported in PEARL-I Subjects Treated with Ombitasvir, Paritaprevir and Ritonavir with or without Ribavirin for 12 weeks (from *Technivie Prescribing Information*)

Adverse Reaction	PEARL-I	
	Ombitasvir, paritaprevir, ritonavir + RBV 12 Weeks N = 91 %	Ombitasvir, paritaprevir, ritonavir 12 Weeks N = 44 %
Asthenia	29	25
Fatigue	15	7
Nausea	14	9
Insomnia	13	5
Pruritus*	7	5
Skin reactions <sup>§,¶</sup>	7	5

\*Grouped term 'pruritus' includes the preferred terms pruritus and pruritus generalized.  
§Grouped term 'skin reactions' includes the preferred terms rash, erythema, eczema, rash maculo-papular, rash macular, dermatitis, rash papular, skin exfoliation, rash pruritic, rash erythematous, rash generalized, dermatitis allergic, dermatitis contact, exfoliative rash, photosensitivity reaction, psoriasis, skin reaction, ulcer and urticaria.  
¶The majority of events were graded as mild in severity. There were no serious events or severe cutaneous reactions, such as Stevens Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), erythema multiforme (EM) or drug rash with eosinophilia and systemic symptoms (DRESS).

Technivie is Pregnancy Category B when administered without ribavirin. Although Technivie has not been studied in pregnant women, animal studies show no evidence of teratogenicity with the administration of ombitasvir (mice and rabbits), paritaprevir or ritonavir (mice and rats) at exposures higher than the recommended clinical dose. When Technivie is administered with ribavirin, the combination regimen is contraindicated in pregnant women and in men whose female partners are pregnant. Unchanged ombitasvir, paritaprevir and its hydrolysis product M13 were the predominant components observed in the milk of lactating rats, without effect on nursing pups. It is not known whether any of the components of Technivie or their metabolites are present in human milk.

Safety and effectiveness of Technivie in pediatric patients less than 18 years of age have not been established. In geriatric patients, no dosage adjustment of Technivie is warranted. No dosage adjustment of Technivie is required in patients with mild, moderate or severe renal impairment; however, Technivie has not been studied in patients on dialysis. No dosage adjustment of Technivie is required in patients with mild hepatic impairment (Child-Pugh A). Technivie is contraindicated in patients with moderate or severe (Child-Pugh B or C) hepatic impairment.

CONTINUED ON NEXT PAGE



**STANDARD COMMERCIAL DRUG FORMULARY  
PRIOR AUTHORIZATION GUIDELINES**

**OMBITASVIR/PARITAPREVIR/RITONAVIR**

**REFERENCES**

- Guidance from the American Association for the Study of Liver Diseases (AASLD) and the Infectious Disease Society of America (IDSA) Recommendations for Testing, Managing, and Treating hepatitis C. Available online at <http://www.hcvguidelines.org/full-report-view> Accessed July 28, 2016.
- Technivie [Prescribing Information]. North Chicago, IL: Abbvie Inc.; February 2017.

Library	Commercial	NSA
Yes	Yes	No

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