TREATMENT OF HEPATITIS C: RECOMMENDATIONS 2016

WHO SHOULD BE TREATED

All treatment-naïve and treatment-experienced patients with compensated or decompensated chronic liver disease related to HCV, who are willing to be treated and who have no contra-indications to treatment, should be considered for therapy[a]

Every person with HCV/HIV co-infection should be considered for treatment when the benefits of therapy outweigh the risks including pre- or post-liver transplantation[b]

Treatment must be considered without delay[a]:

- In patients with significant fibrosis (F2 or F3) or cirrhosis (F4), including decompensated cirrhosis;
- Patients with clinically significant extrahepatic manifestations (e.g. symptomatic vasculitis associated with HCV-related mixed cryoglobulinaemia, HCV immune complex-related nephropathy and non-Hodgkin B cell lymphoma);
- Patients with HCV recurrence after liver transplantation;
- Patients at risk of a rapid evolution of liver disease due to concurrent comorbidities (non-liver solid organ or stem cell transplant recipients, diabetes);
- Individuals at risk of transmitting HCV (active injection drug users, men who have sex with men with high-risk sexual practices, women of childbearing age who wish to get pregnant, haemodialysis patients, incarcerated individuals)

Treatment is not recommended[a]:
In patients with limited life expectancy due to non-liver-related comorbidities

ANTIVIRAL DRUGS FOR HCV TREATMENT

Direct-acting antivirals (DAAs)

Drug, INN (TN)	Product form	Dosage	Dosage and administration, adults**
daclatasvir (Daklinza), generics* available		30 mg, 60 mg, 90 mg	60 mg once a day; with strong CYP450 3A inhibitors - 30 mg once a day; with moderate CYP450 3A inducers - 90 mg once a day
ledipasvir/sofosbuvir (Harvoni), generics available		ledipasvir 90 mg, sofosbuvir 400 mg	1 pill once a day
simeprevir (Olysio, Sovriad), generics available		150 mg	1 pill once a day; used in combination with other drugs
sofosbuvir (Sovaldi), generics available		400 mg	1 pill once a day; used in combination with other drugs
sofosbuvir/velpatasvir (Epclusa), generics available		sofosbuvir 400 mg, velpatasvir 100 mg	1 pill once a day
ombitasvir/paritaprevir/ritonavir + dasabuvir (Viekira Pak)		ombitasvir 12.5 mg, paritaprevir 75 mg, ritonavir 50 mg, dasabuvir 250 mg	2 pills of ombitasvir/paritaprevir/ritonavir once a day + 1 pill of dasabuvir twice a day
elbasvir/grazoprevir (Zepatier)		elbasvir 50 mg, grazoprevir 100 mg	1 pill once a day

Other drugs

pegylated interferon alfa-2a (Pegasys), biosimilars*** available		135 mcg, 180 mcg/0.5 mL in a pre-filled syringe	1.5 mcg/kg per week; used in combination with other drugs
pegylated interferon alfa-2b (PegIntron), biosimilars available		50 mcg, 80 mcg, 120 mcg, 150 mcg/0.5 mL in a pre-filled syringe	1.5 mcg/kg per week; used in combination with other drugs
ribavirin (Rebetol, Copegus), generics available		200 mg	weight-based; used in combination with other drugs

HCV AND HIV DRUG INTERACTIONS[b]

HIV drugs	daclatasvir	elbasvir/ grazoprevir	paritaprevir/ ritonavir/ ombitasvir/ dasabuvir	paritaprevir/ ritonavir/ ombitasvir	simeprevir	sofosbuvir/ ledipasvir	sofosbuvir/ velpatasvir	sofosbuvir
	DAAs							
ATV/r	↑ 110% [i]	↑	↑ 94% [i]	↑ [i]	↑	↑ 8/113%	↑ -/142%	↔
DRV/c	↑	↑	↑	↑	↑	↑ E [i]	↔ [i]	↑
DRV/r	↑ 41%	↑	D [i]	↑ [i]	↑	↑ 34/39% [i]	↓ 28%/- [i]	↑ 34%
LPV/r	↑ 15%	↑	↑	↑	↑	↔ [i]	↓ 29%/-	↔
EFV	↓ 32% [i]	↓ 54/83%	[i]	[i]	↓ 71%	↓ -/34%	↓ -/53%	↑ 6% D4%
ETV	↓	↓	↓ E?	↓ E?	↓	↔	↓	↔
NVP	↓	↓	↓ E?	↓ E?	↓	↔	↓	↔
RPV	↔	↔	E [i]	E [i]	↓ 6% E12%	↔ [i]	↔	↑ 9% E6%
MVC	↔	↔	E	E	↓	E?	E?	↔
DTG	E33%	↔	↔	↔	↔	↔	↔	↔
EVG/c	↑	↑	↑	↑	↑	↑ 36/78%E [i]	↔	↔
RAL	↔	E43%	E134%	E20%	↓ 11% E8%	D≈20%	↔	↓ 5%D 27%
ABC	↔	↔	↔	↔	↔	↔	↔	↔
FTC	↔	↔	↔	↔	↔	↔	↔	↓ 6%
3TC	↔	↔	↔	↔	↔	↔	↔	↔
TAF	↔	E	E	E	↔	E32%	↔	↔
TDF	↑ 10% E10%	↓ 7/14% E34%	↔	↔	↓ 14% E18%	E [i]	E [i]	↓ 6%
ZDV	↔	↔	↔	↔	↔	↔	↔	↔

↑ potential elevated exposure of DAA
↓ potential decreased exposure of DAA
↔ no significant effect
D potential decreased exposure of ARV drug
E potential elevated exposure of ARV drug

No clinically significant interaction expected
These drugs should not be co-administered
Potential interaction which may require a dosage adjustment or close monitoring

Note: the symbol (green, amber, red) used to rank the clinical significance of the drug interaction is based on http://www.hep-druginteractions.org
[i] See http://www.eacsociety.org/files/guidelines_8.1-english.pdf

EASL RECOMMENDATIONS ON TREATMENT OF HEPATITIS C 2016

Treatment recommendations for HCV-monoinfected or HCV/HIV coinfected patients with chronic hepatitis C without cirrhosis, including treatment-naïve patients and patients who failed on a treatment based on pegylated IFN-a and ribavirin (treatment-experienced, DAA-naïve patients)

Patients	Treatment-naïve or -experienced	sofosbuvir/ ledipasvir	sofosbuvir/ velpatasvir	ombitasvir/ paritaprevir/ ritonavir and dasabuvir	ombitasvir/ paritaprevir/ ritonavir	grazoprevir/ elbasvir	sofosbuvir and daclatasvir	sofosbuvir and simeprevir
Genotype 1a	Treatment-naïve	8-12 weeks, no RBV	12 weeks, no RBV	12 weeks, no RBV	No	12 weeks, no RBV if HCV RNA ⩽800,000 (5.9 log) IU/ml or 16 weeks with RBV if HCV RNA >800,000 (5.9 log) IU/ml [2]	12 weeks, no RBV	No
	Treatment-experienced	12 weeks with RBV [1] or 24 weeks, no RBV					12 weeks with RBV [1] or 24 weeks, no RBV	
Genotype 1b	Treatment-naïve	8-12 weeks, no RBV	12 weeks, no RBV	8-12 weeks, no RBV	No	12 weeks, no RBV	12 weeks, no RBV	No
	Treatment-experienced	12 weeks, no RBV		12 weeks, no RBV				
Genotype 2	Both	No	12 weeks, no RBV	No	No	No	12 weeks, no RBV	No
Genotype 3	Treatment-naïve	No	12 weeks, no RBV	No	No	No	12 weeks, no RBV	No
	Treatment-experienced		12 weeks with RBV [3] or 24 weeks, no RBV				12 weeks with RBV [3] or 24 weeks, no RBV	
Genotype 4	Treatment-naïve	12 weeks, no RBV	12 weeks, no RBV	No	12 weeks, with RBV	12 weeks, no RBV	12 weeks, no RBV	12 weeks, no RBV
	Treatment-experienced	12 weeks with RBV or 24 weeks, no RBV				12 weeks, no RBV if HCV RNA ⩽800,000 (5.9 log) IU/ml or 16 weeks with RBV if HCV RNA >800,000 (5.9 log) IU/ml [2]	12 week with RBV or 24 week, no RBV	12 weeks with RBV or 24 weeks, no RBV
Genotype 5 or 6	Treatment-naïve	12 weeks, no RBV	12 weeks, no RBV	No	No	No	12 weeks, no RBV	No
	Treatment-experienced	12 weeks with RBV or 24 weeks, no RBV					12 weeks with RBV or 24 weeks, no RBV	

Treatment recommendations for HCV-monoinfected or HCV/HIV coinfected patients with chronic hepatitis C with compensated (Child-Pugh A) cirrhosis, including treatment-naïve patients and patients who failed on a treatment based on pegylated IFN-a and ribavirin (treatment-experienced, DAA-naïve patients)

Patients	Treatment-naïve or -experienced	sofosbuvir/ ledipasvir	sofosbuvir/ velpatasvir	ombitasvir/ paritaprevir/ ritonavir and dasabuvir	ombitasvir/ paritaprevir/ ritonavir	grazoprevir/ elbasvir	sofosbuvir and daclatasvir	sofosbuvir and simeprevir
Genotype 1a	Treatment-naïve	12 weeks, no RBV	12 weeks, no RBV	24 weeks, no RBV	No	12 weeks, no RBV if HCV RNA ⩽800,000 (5.9 log) IU/ml or 16 weeks with RBV if HCV RNA >800,000 (5.9 log) IU/ml [2]	12 weeks, no RBV	No
	Treatment-experienced	12 weeks with RBV [1] or 24 weeks, no RBV					12 weeks with RBV [1] or 24 weeks, no RBV	
Genotype 1b	Treatment-naïve	12 weeks, no RBV	12 weeks, no RBV	12 weeks, no RBV	No	12 weeks, no RBV	12 weeks, no RBV	No
	Treatment-experienced							
Genotype 2	Both	No	12 weeks, no RBV	No	No	No	12 weeks, no RBV	No
Genotype 3	Treatment-naïve	No	12 weeks, no RBV	No	No	No	24 weeks, no RBV	No
	Treatment-experienced		12 weeks with RBV [3] or 24 weeks, no RBV					
Genotype 4	Treatment-naïve	12 weeks, no RBV	12 weeks, no RBV	No	12 weeks, with RBV	12 weeks, no RBV	12 weeks, no RBV	12 weeks, no RBV
	Treatment-experienced	12 weeks with RBV or 24 weeks, no RBV				12 weeks, no RBV if HCV RNA ⩽800,000 (5.9 log) IU/ml or 16 weeks with RBV if HCV RNA >800,000 (5.9 log) IU/ml [2]	12 weeks with RBV or 24 weeks, no RBV	12 weeks with RBV or 24 weeks, no RBV
Genotype 5 or 6	Treatment-naïve	12 weeks, no RBV	12 weeks, no RBV	No	No	No	12 weeks, no RBV	No
	Treatment-experienced	12 weeks with RBV or 24 weeks, no RBV					12 weeks with RBV or 24 weeks, no RBV	

[1] Add ribavirin only in patients with RASs that confer high-level resistance to NS5A inhibitors at baseline if RAS testing available.
[2] Prolong to 16 weeks and add ribavirin only in patients with RASs that confer resistance to elbasvir at baseline if RAS testing available.
[3] Add ribavirin only in patients with NS5A RAS Y93H at baseline if RAS testing available.

HCV TREATMENT OPTIONS IN HCV/HIV CO-INFECTED PERSONS, EUROPEAN AIDS CLINICAL SOCIETY GUIDELINES, V. 8.1, OCTOBER 2016

Genotype	Treatment regimen	Non-cirrhotic	Compensated cirrhotic	Decompensated cirrhotics CTP class B/C
		Treatment regimen, treatment duration & ribavirin usage		
1 & 4	SOF + SMP +/- RBV	GT 4 only: 12 weeks with RBV or 24 weeks without RBV(i)		Not recommended
	SOF/LDV +/- RBV	8 weeks without RBV(ii) or 12 weeks +/- RBV(iii)	12 weeks +/- RBV or 24 weeks without RBV(iv)	
	SOF + DCV +/- RBV	12 weeks +/- RBV(iii)	12 weeks +/- RBV or 24 weeks without RBV(iv)	
	SOF + VEL	12 weeks		12 weeks with RBV
	OBV/PTV/r + DSV	8(v)-12 weeks in GT 1b	12 weeks in GT 1b	Not recommended
	OBV/PTV/r + DSV + RBV	12 weeks in GT 1a	24 weeks in GT 1a	Not recommended
	OBV/PTV/r + RBV	12 weeks in GT 4		Not recommended
	EBR + GZR	12 weeks(vi)		Not recommended
2	SOF + DCV	12 weeks		12 weeks with RBV
	SOF + VEL	12 weeks		12 weeks with RBV
3	SOF + DCV +/- RBV	12 weeks +/- RBV(vii) or 24 weeks without RBV	24 weeks with RBV	
	SOF + VEL +/- RBV	12 weeks +/- RBV(vii) or 24 weeks without RBV		24 weeks with RBV
5 & 6	SOF/LDV +/- RBV	12 weeks +/- RBV or 24 weeks without RBV(i)	12 weeks with RBV or 24 weeks without RBV(i)	12 weeks with RBV or 24 weeks without RBV
	SOF + DCV +/- RBV	12 weeks +/- RBV or 24 weeks without RBV(i)	12 weeks with RBV or 24 weeks without RBV(i)	12 weeks with RBV or 24 weeks without RBV
	SOF + VEL	12 weeks		12 weeks with RBV

DCV = daclatasvir, DSV = dasabuvir, EBR = elbasvir, GZR = grazoprevir
LDV = ledipasvir, OBV = ombitasvir, PTV/r = paritaprevir/RTV, RBV = ribavirin
SMP = simeprevir, SOF = sofosbuvir, VEL = velpatasvir, RAS = Resistance Associated Substitutions

(i) In treatment experienced persons RBV treatment for 12 weeks or prolong treatment to 24 weeks without RBV
(ii) 8 weeks treatment without RBV only in treatment-naïve persons with F< 3 and baseline HCV-RNA < 6 million IU/mL
(iii) Addition of RBV in GT1a treatment experienced persons, but not in persons without NS5A RASs, if RASs testing is available
(iv) RBV can be avoided in GT1b, GT4 treatment-naïve, GT1a treatment-naïve and in GT1a experienced persons without NS5A RASs, if RASs testing is available; in persons intolerant to RBV, treatment may be prolonged to 24 weeks
(v) 8 weeks treatment without RBV only in persons without cirrhosis
(vi) Extension of treatment to 16 weeks and addition of RBV in persons with GT1a with baseline HCV-RNA > 800.000 IU/mL and NS5A RASs and in HCV GT4 experienced persons with HCV-RNA > 800.000 IU/mL
(vii) Addition of RBV only in treatment experienced persons with baseline NS5A RASs, if RAS testing available; if these persons are intolerant to RBV treatment may be prolonged to 24 weeks without RBV

SEVT

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