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Operațiunea: Îmbunătățirea nivelului de competențe al profesioniștilor din sectorul medical

Titlu: „Optimizarea prevenției și tratamentului Hepatitelor cronice B și C prin creșterea competențelor personalului medical din România”

Contract: POCU 91/4/8/106781

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Medicatia antivirala DAA recomandata pentru genotipul 1 a

Pana in anul 2018 au fost aprobate 4 medicamente DAA echivalente ca eficeinta, pentru terapia hepatitei cronice C la pacientul cu infectie cu genotipul 1a: Sofosbuvir/Ledipasvir, Grazoprevir/Elbasvir, Sofosbuvir/Velpatasvir, Glecaprevir/Pibrentasvir. **Tabel 1, 2, 3** (Recommendations on Treatment of Hepatitis C, European Association for the Study of the Liver. EASL. *J Hepatol*, 2018)

Dozele recomandate /zi sunt fixe:

- sofosbuvir 400mg si velpatasvir 100mg/zi, echivalent cu doza dintr-o tableta
- glecaprevir 300mg si pibrentasvir 120mg/zi, adica 3 tablete/zi, administrate 1 data /zi (1 tb continand 100 mg glecaprevir si 40 mg pibrentasvir)
- sofosbuvir 400mg si ledipasvir 90 mg/zi, adica 1 tb/zi
- grazoprevir 100mg si elbasvir 50mg/zi, adica 1 tb/zi

Combinatia pangenotipica: sofosbuvir/velpatasvir este recomandata pacientilor tratament naivi si experimentati, fara ciroza sau cu ciroza compensata- CHILD A, pe o durata de 12 saptamani, cu SVR de 98% conform unor studii, pentru pacientii non HIV si 95% pentru pacientii coinfectie HIV. (Recommendations on Treatment of Hepatitis C, European Association for the Study of the Liver. EASL. *J Hepatol*, 2018, Feld JJ, Jacobson IM, Hezode C, Asselah T, Ruane PJ, Gruener N, et al. Sofosbuvir and velpatasvir for HCV Genotype 1, 2, 4, 5, and 6 infection. *N Engl J Med* 2015)

SVR dupa terapia cu sofosbuvir/velpatasvir, 12 saptamani pentru genotipul 1a, este superior terapiei de 8 saptamani cu combinatie tripla: sofosbuvir/velpatasvir/voxilaprevir (99% vs 92%), motiv pentru care aceasta

din urma nu se recomanda pentru genotipul 1a. (Tsai N, Bacon B, Curry M, Dieterich D, Flamm S, Kowdley K, et al. Utilization of DAA therapies ledipasvir/sofosbuvir and sofosbuvir/velpatasvir in patients with genotype 1 HCV: real-world experience from the TRIO network. *J Hepatol* 2017)

Tabel 1. Conform Recommendations on Treatment of Hepatitis C, European Association for the Study of the Liver. EASL. *J Hepatol*, 2018.

Terapia pacientilor naivi (netratati anterior) sau experimentati (tratati anterior cu combinatii de interferon alfa standard sau pegilat, ribavirina sau sofosbuvir), cu sau fara ciroza compensata Child-Pough A, recomandat in functie de genotip si subtip

Genotype	Pangenotypic regimens			Genotype-specific regimens		
	SOF/ VEL	GLE/PIB	SOF/ VEL/ VOX	SOF/ LDV	GZR/ EBR	OBV/ PTV/r + DSV
Genotype 1a	Yes	Yes	No*	Yes ^a	Yes ^b	No
Genotype 1b	Yes	Yes	No*	Yes	Yes	Yes
Genotype 2	Yes	Yes	No*	No	No	No
Genotype 3	Yes ^c	Yes	Yes ^d	No	No	No
Genotype 4	Yes	Yes	No*	Yes ^a	Yes ^a	No
Genotype 5	Yes	Yes	No*	Yes ^a	No	No
Genotype 6	Yes	Yes	No*	Yes ^a	No	No

DSV, dasabuvir; EBR, elbasvir; GLE, glecaprevir; GZR, grazoprevir; IFN, interferon; LDV, ledipasvir; OBV, ombitasvir; PIB, pibrentasvir; PTV, paritaprevir; r, ritonavir; SOF, sofosbuvir; VEL, velpatasvir; VOX: voxilaprevir.

* combinatia de trei medicamente, este efecienta, dar mai putin utilizata avand in vedere eficienta similara a combinatiei de doua medicamente

^a terapia pacientilor naivi fara ciroza sau cu ciroza compensata Child-Pugh A

^b terapia pacientilor naivi si experimentati fara ciroza sau cu ciroza compensata Child-Pugh A, cu ARN VHC $\leq 800,000$ IU/ml (5.9 Log_{10} IU/ml)

^c terapia pacientilor naivi si experimentati fara ciroza

^d terapia pacientilor naivi si experimentati cu ciroza compensata Child-Pugh A

^e terapia pacientilor naivi fara ciroza sau cu ciroza compensata Child-Pugh A, cu ARN VHC $\leq 800,000$ IU/ml (5.9 Log_{10} IU/ml).

Tabel 2. Conform Recommendations on Treatment of Hepatitis C, European Association for the Study of the Liver. EASL. J Hepatol, 2018.

Terapia recomandată pacienților cu hepatita cronică C monoinfecție sau coinfectie HIV, fără ciroză, neexperimentați (naivi, netratați anterior) sau pretratați cu interferon și ribavirină, dar netratați cu DAA

Patients	Prior treatment experience	SOF/VEL	GLE/PIB	SOF/VEL/VOX	SOF/LDV	GZR/EBR	OBV/PTV/r + DSV
Genotype 1a	Treatment-naïve	12 wk	8 wk	No	8-12 wk	12 wk (HCV RNA \leq 800,000 IU/ml)	No
	Treatment-experienced	12 wk	8 wk	No	No	12 wk (HCV RNA \leq 800,000 IU/ml)	No
Genotype 1b	Treatment-naïve	12 wk	8 wk	No	8-12 wk	8 wk (F0-F2) 12 wk (F3)	8 wk (F0-F2) 12 wk (F3)
	Treatment-experienced	12 wk	8 wk	No	12 wk	12 wk	12 wk
Genotype 2	Treatment-naïve	12 wk	8 wk	No	No	No	No
	Treatment-experienced	12 wk	8 wk	No	No	No	No
Genotype 3	Treatment-naïve	12 wk	8 wk	No	No	No	No
	Treatment-experienced	12 wk	12 wk	No	No	No	No
Genotype 4	Treatment-naïve	12 wk	8 wk	No	12 wk	12 wk (HCV RNA \leq 800,000 IU/ml)	No
	Treatment-experienced	12 wk	8 wk	No	No	No	No
Genotype 5	Treatment-naïve	12 wk	8 wk	No	12 wk	No	No
	Treatment-experienced	12 wk	8 wk	No	No	No	No
Genotype 6	Treatment-naïve	12 wk	8 wk	No	12 wk	No	No
	Treatment-experienced	12 wk	8 wk	No	No	No	No

DAA, direct-acting antiviral; DSV, dasabuvir; EBR, elbasvir; GLE, glecaprevir; GZR, grazoprevir; HCV, hepatitis C virus; HIV, human immunodeficiency virus; LDV, ledipasvir; OBV, ombitasvir; PIB, pibrentasvir; PTV, paritaprevir; r, ritonavir; SOF, sofosbuvir; VEL, velpatasvir; VOX: voxilaprevir.

Tabel 3. Conform Recommendations on Treatment of Hepatitis C, European Association for the Study of the Liver. EASL. *J Hepatol*, 2018.

Terapia recomandata pacientilor cu hepatita cronica C monoinfectie sau coinfectie HIV, cu ciroza compensata Child-Pough A, neexperimentati (naivi, netratati anterior) sau pretratati cu interferon si ribavirina, dar netratati cu DAA

Patients	Prior treatment experience	SOFVEL	GLE/PIB	SOFVEL/VOX	SOF/LDV	GZR/EBR	OBV/PTV/r + DSV
Genotype 1a	Treatment-naïve	12 wk	12 wk	No	12 wk	12 wk (HCV RNA ≤800,000 IU/ml)	No
	Treatment-experienced	12 wk	12 wk	No	No	12 wk (HCV RNA ≤800,000 IU/ml)	No
Genotype 1b	Treatment-naïve	12 wk	12 wk	No	12 wk	12 wk	12 wk
	Treatment-experienced	12 wk	12 wk	No	12 wk	12 wk	12 wk
Genotype 2	Treatment-naïve	12 wk	12 wk	No	No	No	No
	Treatment-experienced	12 wk	12 wk	No	No	No	No
Genotype 3	Treatment-naïve	No	12 wk	12 wk	No	No	No
	Treatment-experienced	No	16 wk	12 wk	No	No	No
Genotype 4	Treatment-naïve	12 wk	12 wk	No	12 wk	12 wk (HCV RNA ≤800,000 IU/ml)	No
	Treatment-experienced	12 wk	12 wk	No	No	No	No
Genotype 5	Treatment-naïve	12 wk	12 wk	No	12 wk	No	No
	Treatment-experienced	12 wk	12 wk	No	No	No	No
Genotype 6	Treatment-naïve	12 wk	12 wk	No	12 wk	No	No
	Treatment-experienced	12 wk	12 wk	No	No	No	No

DAA, direct-acting antiviral; DSV, dasabuvir; EBR, elbasvir; GLE, glecaprevir; GZR, grazoprevir; HCV, hepatitis C virus; HIV, human immunodeficiency virus; LDV, ledipasvir; OBV, ombitasvir; PIB, pibrentasvir; PTV, paritaprevir; r, ritonavir; SOF, sofosbuvir; VEL, velpatasvir; VOX: voxilaprevir.



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