GILEAD | Medical Information

Hepcludex® (bulevirtide-gmod) Effect on Patient-Reported Outcomes

This document is in response to your request for information regarding the effect of Hepcludex® (bulevirtide-gmod [BLV]) on patient-reported outcomes (PROs) for the treatment of chronic HDV infection.

Some data may be outside of the US FDA-approved prescribing information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA-approved prescribing information.

The full indication, important safety information, and boxed warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/hdv/hepcludex/hepcludex_pi.

Summary

Product Labeling[1]

There are no data in the US FDA-approved prescribing information regarding the effect of BLV on PROs related to the treatment of chronic HDV.

BLV is indicated for the treatment of chronic HDV infection in adults without cirrhosis or with compensated cirrhosis.

This indication is approved under accelerated approval based on a decrease in HDV RNA and ALT normalization. An improvement in disease-related clinical outcomes has not been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

The recommended dosage in adults is BLV 8.5 mg once daily administered by SUBQ injection.

The efficacy of BLV once daily in the treatment of adults with chronic HDV infection without cirrhosis or with compensated cirrhosis is based on data through Week 144 from a multicenter, randomized, open-label, parallel-arm phase 3 trial, Trial MYR301 (NCT03852719), in which 100 participants received BLV 8.5 mg once daily. The MYR301 protocol specified the BLV dose as 10 mg; however, a dose recovery study later showed that the delivered dose was 8.5 mg.

Clinical Data on the Effect of BLV on PROs

MYR301, a phase 3 study, evaluated the safety and efficacy of BLV 2 mg or 10 mg compared with delayed treatment (no treatment for 48 weeks) in adult participants with HDV (N=150).[2] A prespecified exploratory analysis was performed using the HQLQ, FSS, and EQ-5D-3L instruments to assess the effect of BLV treatment on quality of life.[3]

- Through Week 48, several domains of the HQLQ and EQ-5D-3L questionnaire demonstrated improved outcomes in participants who received BLV 2 mg or 10 mg vs delayed treatment. FSS scores were stable across the analysis period, regardless of treatment arm and cirrhosis status.[3]

- In an exploratory analysis of HQLQ results from the BLV 2 mg arm, participants had a ≥3-point improvement from baseline to Week 144 in all domains except the physical component of the summary domain. The greatest improvements (≥10 points) were reported in the hepatitis-specific limitations and hepatitis-specific health distress improvements domains. Most domain scores showed continued improvement from Week 48 to Weeks 96 and/or 144.[4]

Real-World Data on the Effect of BLV on PROs

In a cross-sectional survey that used retrospective data from the Adelphi Real-World Hepatitis Disease Specific Programme to compare PROs of patients who received BLV with those of patients who were either treatment naive or received another treatment for HDV, patients who received BLV had significantly improved HBQOL scores across most domains compared with patients who were treatment-naive or received other treatment for HDV. There were no significant between-group differences in scores on the EQ-5D-5L, EQ-5D VAS, WPAI, and FSS.[5]

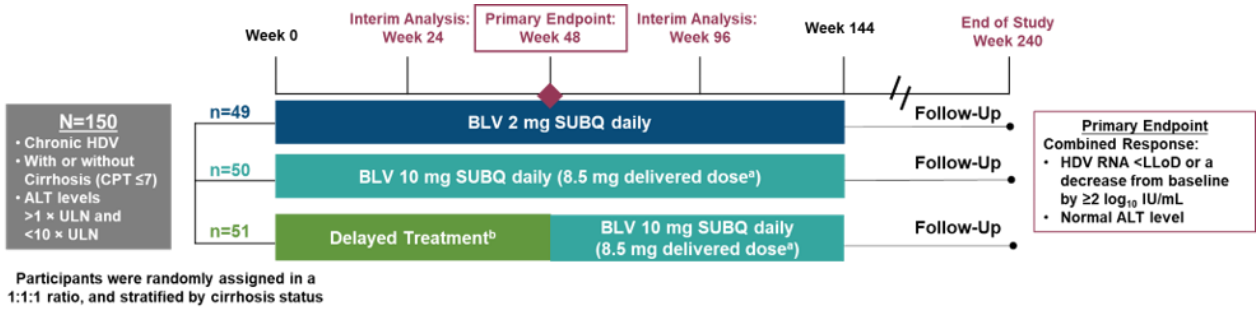
Clinical Data on the Effect of BLV on PROs

Study Design and Demographics

MYR301 was an open-label, multicenter, randomized, phase 3 study that evaluated the safety and efficacy of immediate treatment with BLV 2 mg or 10 mg compared with delayed treatment with BLV 10 mg (no treatment for 48 weeks) in participants with chronic HDV (N=150; Table 1).[2]

The primary endpoint was the combined response of undetectable (<LLOD) HDV RNA or a decrease of ≥2 $\log_{10}$ IU/mL from baseline and ALT level normalization at Week 48. Other endpoints included the following: rates of undetectable HDV RNA levels; rates of ALT normalization; and change from baseline in liver stiffness measurement, as measured by elastography.[6-9]

Figure 1. MYR301: Study Design[7]



Abbreviations: ULN=upper limit of normal.
[a]The MYR301 protocol specified the dose as 10 mg per vial, and the delivered dose was 8.5 mg.
[b]Participants in the delayed treatment arm did not receive BLV treatment through Week 48.

Table 1. MYR301: Baseline Demographics and Disease Characteristics[7]

Key Demographics and Characteristics	Delayed Treatment BLV 10 mg (n=51)	BLV 2 mg (n=49)	BLV 10 mg (n=50)
Age, mean ± SD, years	41±7.5	44±9	41±8.5
Male, n (%)	26 (51)	30 (61)	30 (60)

Key Demographics and Characteristics		Delayed Treatment BLV 10 mg (n=51)	BLV 2 mg (n=49)	BLV 10 mg (n=50)
Race, n (%)	White	40 (78)	41 (84)	43 (86)
	Asian	11 (22)	8 (16)	6 (12)
	Black	0	0	1 (2)
Cirrhosis,[a] n (%)		24 (47)	23 (47)	24 (48)
Liver stiffness measurement,[b] mean ± SD, kPa		15±9	14±8.2	15±9.3
HDV RNA, mean ± SD, log_{10} IU/mL		5.1±1.36	5±1.32[c]	5.1±1.4
HDV GT, 1/5, n (%)		51 (100)/0	49 (100)/0	48 (96)[c]/1 (2)
HBV DNA, mean ± SD, log_{10} IU/mL		0.9±0.99	1.3±1.3[c]	1.1±1.26[c]
HBeAg not detected, n (%)		47 (92)	45 (92)	43 (86)
HBsAg, mean ± SD, log_{10} IU/mL		3.7±0.47	3.7±0.52	3.6±0.59
HBV GT, n (%)	A/D/E	4 (8)/39 (77)/0	2 (4)/44 (90)/0	3 (6)/43 (86)/1 (2)
	Could not be determined	8 (16)	3 (6)	3 (6)
ALT level, mean ± SD, U/L		102±61.9	108±62.5	123±80.6
Previous interferon therapy, n (%)		29 (57)	26 (53)	29 (58)
Concomitant HBV nucleo(t)side analog treatment, n (%)		32 (63)	31 (63)	27 (54)

Abbreviations: GT=genotype; HBeAg=hepatitis B envelope antigen; HBsAg=hepatitis B surface antigen.
[a]According to CPT, Class A cirrhosis (ie, scores of 5 or 6) correlates with mildly impaired liver function; Class B (ie, scores of 7 to 9) correlates with moderately impaired liver function; and Class C (ie, scores of 10 to 15) correlates with severely impaired liver function.
[b]Assessed using transient elastography (FibroScan, Echosens; range: 2.5–7.5 kPa; higher levels indicate more severe liver scarring).
[c]One participant had missing data.

PROs

A prespecified exploratory analysis was performed to evaluate the effect of BLV treatment through 48 weeks using several PRO instruments.[3]

- HQLQ: Consists of eight scales of the SF-36 instrument and 15 generic disease-specific items (score range, 0–100; higher scores indicate better health).
- FSS: Consists of a nine-item questionnaire regarding fatigue (score range, 1–7; higher scores indicate greater fatigue).
- EQ-5D-3L: Consists of two parts including descriptive scores from a questionnaire (five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression; severity on each dimension is rated as “no,” “some,” or “extreme” problems) and a VAS (rating of current health status; score range, 0–100; a score of 0 indicates worst imaginable health status, and a score of 100 indicates the best imaginable health status).

Each PRO instrument was completed at baseline and Weeks 24 and 48. Subgroup analysis was performed by cirrhosis status at baseline; however, statistical testing was not performed for these post hoc analyses.[3]

Baseline scores from each instrument were generally comparable across treatment arms: HQLQ, mean baseline scores were >50 in each domain; FSS, mean fatigue scores were <5; and EQ-5D-3L, higher rates of participants reported “some problems” with pain/discomfort and anxiety/depression dimensions than with mobility, self-care, and usual activities dimensions. All baseline PRO scores are shown in Table 2.[3]

Table 2. MYR301: Baseline PRO Scores[3]

PROs		Delayed Treatment BLV 10 mg (n=51)	BLV 2 mg (n=49)	BLV 10 mg (n=50)
HQLQ domain score, mean ± SD	Physical functioning	79.3±21.59	84.6±15.17	82.6±16.94
	Role physical	71±25.95	76.7±19.3	69.6±22.9
	Bodily pain	78.5±24.51	78±24.31	73.2±26.73
	General health	53.8±20.19	59.1±19.39	56.1±16.87
	Vitality	57.9±20.18	60.7±19.18	58.7±17.21
	Social functioning	75.7±24.29	79.1±22.15	75.3±19.64
	Role emotional	74.2±26.52	74.7±24.82	74.3±25.08
	Mental health	64.6±18.73	66.2±17.66	68.2±15.23
	Physical component summary	50.3±7.49	52.3±5.69	49.9±6.28
	Mental component summary	45.5±10.09	45.9±10.14	46.4±8.76
	Health distress	58.3±26.85[a]	61.1±22.62	58.1±22.86[a]
	Positive well-being	58.8±22.4	66.1±19.16	58.3±20.64
	Health-specific limitations	70.6±28.73	75.8±24.82	72.5±23.56[a]
	Health-specific health distress	52.4±29.99	56±26.22	54.8±26.6[b]
FSS score, mean ± SD		4.2±1.59	3.6±1.57	3.7±1.41[a]
EQ-5D-3L dimensions and VAS				
Mobility, n (%)[b]	No problems	41 (80.4)	42 (85.7)	40 (80)
	Some problems	10 (19.6)	7 (14.3)	8 (16)
	Extreme problems	0	0	0
Self-care, n (%)[b]	No problems	47 (92.2)	46 (93.9)	46 (92)
	Some problems	4 (7.8)	3 (6.1)	2 (4)
	Extreme problems	0	0	0
Usual activities, n (%)[b]	No problems	36 (70.6)	39 (79.6)	38 (76)
	Some problems	15 (29.4)	10 (20.4)	10 (20)
	Extreme problems	0	0	0
Pain/ discomfort, n (%)[b]	No problems	25 (49)	27 (55.1)	28 (56)
	Some problems	25 (49)	22 (44.9)	20 (40)
	Extreme problems	1 (2)	0	0
Anxiety/ depression, n (%)[b]	No problems	25 (49)	25 (51)	26 (52)
	Some problems	24 (47.1)	23 (46.9)	22 (44)
	Extreme problems	2 (3.9)	1 (2)	0
VAS score, mean ± SD		72±18.4	73.1±16.2[a]	73.9±19.3[c]

[a]Data were missing for 1 participant.
[b]Data were missing for 2 participants in the 10 mg BLV group.
[c]Data were missing for 5 participants.

Results at Week 48[3]

HQLQ

Significant improvements from baseline to Week 48 in HQLQ scores were noted for BLV 2 mg vs delayed treatment arms in the following domains (each, $P<0.05$): role physical (LSM TD, 8.3), hepatitis-specific limitations (LSM TD, 7.5), and hepatitis-specific distress (LSM TD, 9.4). Similarly, significant improvements were noted for the BLV 10 mg vs delayed treatment arms in the role physical (LSM TD, 8), role emotional (LSM TD, 7.9), and physical component summary (LSM TD, 2.5) domains (each, $P<0.05$).

Regardless of cirrhosis status, participants treated with BLV vs delayed treatment had numerical improvements in several domains of the HQLQ. Among participants with cirrhosis, numerically greater improvements were noted for the BLV 10 mg arm vs the delayed treatment arm in the following domains: physical functioning, role physical, bodily pain,

general health, physical component summary, hepatitis-specific limitations, and hepatitis-specific health distress. Among participants without cirrhosis, those in the 2- and 10-mg BLV arms each had greater improvements from baseline than the delayed treatment arm in 13 of the 14 domains; the increase in the general health domain score was higher in the BLV 2 mg arm than in the delayed treatment arm.

FSS

Regardless of the treatment arm or cirrhosis status, all participants had comparable assessments of fatigue with the FSS at baseline, Week 24, and Week 48; there were non-significant differences in LSMs for BLV 2 mg (-0.35; *P*=0.21) and 10 mg arms (-0.26; *P*=0.365) vs delayed treatment arms at Week 48.

EQ-5D-3L

Relative to the delayed treatment arm, the BLV 2 mg or 10 mg arm had a greater likelihood of improvement in the anxiety/depression and self-care dimensions of the EQ-5D-3L questionnaire. The BLV 2 mg arm had a significantly greater likelihood of reporting improvement in the anxiety/depression dimension at Week 24 in than the delayed treatment arm (Table 3).

Table 3. MYR301: Comparisons in EQ-5D-3L Dimensions Between the BLV Arms and the Delayed Treatment Arm at Weeks 24 and 48[3]

EQ-5D-3L Dimensions		Week 24			Week 48		
		Delayed Treatment	BLV 2 mg	BLV 10 mg	Delayed Treatment	BLV 2 mg	BLV 10 mg
Mobility	n	47	48	45	50	48	44
	OR (95% CI); *P*-value	–	2.1 (0.5–8.4); 0.319	1.1 (0.3–4.1); 0.856	–	1.7 (0.6–5.2); 0.323	2 (0.6–6.2); 0.244
Self-care	n	47	48	45	50	47	44
	OR (95% CI); *P*-value	–	4.6 (0.4–50.2); 0.209	3.6 (0.3–39); 0.286	–	2.8 (0.3–30.3); 0.394	2.4 (0.2–26); 0.47
Usual activities	n	47	48	45	50	48	44
	OR (95% CI); *P*-value	–	1.7 (0.6–5.1); 0.345	0.7 (0.3–1.9); 0.487	–	2.3 (0.8–6.8); 0.122	1.1 (0.4–2.9); 0.912
Pain/ discomfort	n	47	48	45	50	48	44
	OR (95% CI); *P*-value	–	1.9 (0.7–4.6); 0.188	0.8 (0.3–2); 0.611	–	1.7 (0.7–4.1); 0.268	1.5 (0.6–3.8); 0.385
Anxiety/ depression	n	47	48	45	50	48	44
	OR (95% CI); *P*-value	–	4 (1.5–10.8); 0.007	1.7 (0.7–4.5); 0.267	–	1.4 (0.6–3.6); 0.441	1.3 (0.5–3.3); 0.59)

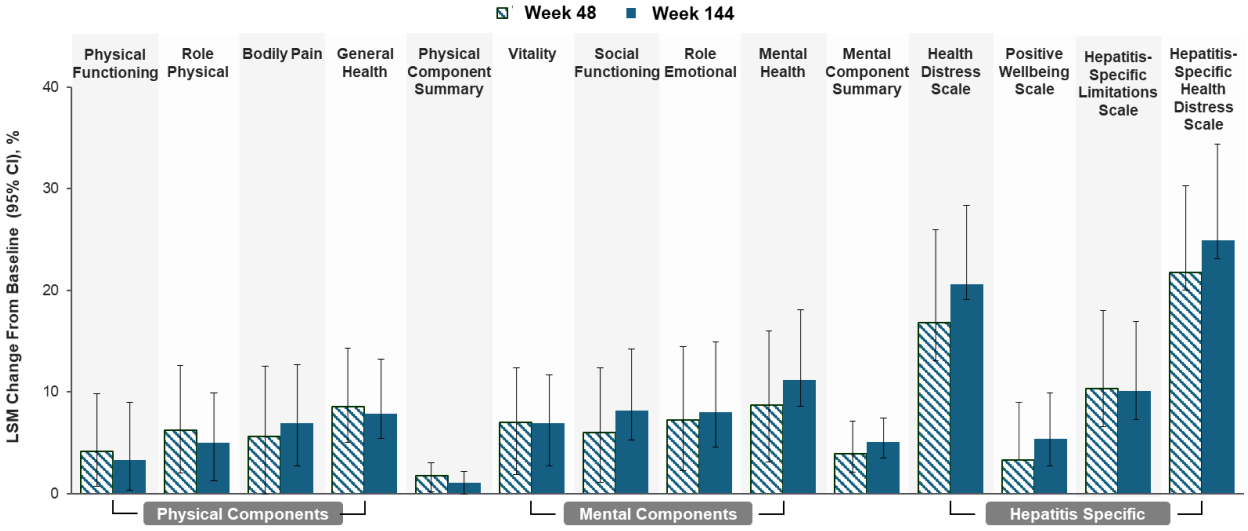
Regardless of the treatment arm or cirrhosis status, most participants had no shifts from “no” to “some” problems (and vice versa) across all dimensions from baseline to Week 48. Within the usual activities dimension, more participants with cirrhosis had shifts from “no” to “some problems” than those without cirrhosis (16.9% vs 6.3%, respectively).

The arithmetic mean change from baseline to Week 48 in EQ-5D-3L VAS scores was greater among participants in the BLV 2 mg arm than among those in the delayed treatment arm (LSM TD, 5.3; *P*=0.047); numerically higher changes were noted in the BLV 2 mg arm, regardless of cirrhosis status. Conversely, arithmetic mean changes from baseline to Week 48 in EQ-5D-3L VAS scores were numerically similar between the BLV 10 mg and delayed treatment arms (LSM TD, -0.6; *P*=0.818); these results were consistent within the subgroups of participants with and without cirrhosis.

Exploratory analysis: HQLQ results from the BLV 2 mg arm through Week 144[4]

An exploratory analysis was performed using HQLQ outcomes collected from participants within the 2 mg BLV arm who had data through Week 144. Four participants in the BLV 2 mg arm dropped out of the study by Week 144 and were excluded from this analysis. Participants had a ≥3-point improvement from baseline to Week 144 in all domains of the HQLQ except the physical component of the summary domain (Figure 2). The greatest improvements (≥10 points) were reported in the hepatitis-specific limitations and hepatitis-specific health distress improvements domains; improvements ≥5 points were reported for 12 of the 14 domains. Most domain scores showed continued improvement from Week 48 to Weeks 96 and/or 144.

Figure 2. MYR301: Changes in HQLQ Scores From Baseline to Weeks 48 and 144[4]



Real-World Data on the Effect of BLV on PROs

Retrospective European Study[5]

Study design and demographics

A retrospective study that used data from the Adelphi Real-World Hepatitis Disease Specific Programme compared HRQOL outcomes of patients with HDV who received BLV treatment with those of patients who were either treatment naive or received treatment other than BLV for HDV across Europe and the UK (N=553). Patients could complete the following PROs: HBQOL, EQ-5D VAS, EQ-5D-5L, WPAI, and FSS. Baseline demographics are summarized in Table 4.

Table 4. Baseline Demographics and Disease Characteristics (Buti et al)[5]

Key Demographics and Characteristics	BLV (n=363)	Treatment-Naive or Other Treatment (n=190)
Age, median (Q1, Q3), years	41 (33, 51)	45 (36, 56)
Male, n (%)	257 (71)	122 (66)

Key Demographics and Characteristics		BLV (n=363)	Treatment-Naive or Other Treatment (n=190)
Race,[a] n (%)	White	191 (73)	118 (69)
	Black African or Caribbean	28 (11)	26 (15)
	Other[b]	43 (16)	27 (16)
Most recent ALT,[c] median (Q1, Q3), U/L		60 (37, 126)	49 (33, 83)
Fibrosis score,[d] F0/F1/F2/F3/F4, n (%)		45 (13)/80 (24)/ 124 (37)/48 (14)/ 39 (12)	32 (20)/ 37 (24)/ 40 (25)/ 23 (15)/ 25 (16)

Abbreviation: Q=quarter.
[a]Multiple race categories could be selected. Patient-reported race was not collected in France. BLV, n=262; treatment-naive or other, n=171.
[b]Other included East or Southeast Asian, South Asian (Indian subcontinent), Middle Eastern or North African, and other.
[c]BLV, n=250; treatment-naive or other, n=133.
[d]BLV, n=336; treatment-naive or other, n=157.

Results

Patients who received BLV had significantly improved HBQOL scores across most dimensions compared with patients who were treatment naive or received other treatment for HDV: global (*P*=0.005), anticipation anxiety (*P*=0.01), vitality (*P*=0.004), stigma (*P*=0.017), vulnerability (*P*=0.017), transmission (*P*=0.014), and viral response (*P*=0.018).

There were no differences between groups in the EQ-5D-5L, EQ-5D VAS, WPAI, or FSS scores.

References

1. Enclosed. Gilead Sciences Inc. HEPCLUDEX® (bulevirtide-gmod) injection, for subcutaneous use. US Prescribing Information. Foster City, CA.
2. Wedemeyer H, Aleman S, Blank A, et al. Final Results of MYR301: A Randomised Phase 3 Study Evaluating the Efficacy and Safety of BLV Monotherapy for Chronic Hepatitis Delta. [Presentation #LBO-004]. Paper presented at: European Association for the Study of the Liver; May 7–10, 2025; Amsterdam, the Netherlands.
3. Buti M, Wedemeyer H, Aleman S, et al. Patient-reported outcomes in chronic hepatitis delta: An exploratory analysis of the phase III MYR301 trial of bulevirtide [Main Body + Supplement]. *J Hepatol.* 2025;82(1):28-36.
4. Buti M, Wedemeyer H, Aleman S, et al. Patient-Reported Outcomes Among Patients With Chronic Hepatitis Delta Treated With Bulevirtide 2 mg: A Long-Term Analysis of the Phase 3 MYR301 Trial at 144 Weeks [Poster 1193]. Paper presented at: The Liver Meeting, American Association for the Study of Liver Diseases (AASLD); November 15 – 19, 2024; San Diego, CA.
5. Buti M, Hennessy F, Pennant T, et al. Impact of Bulevirtide Treatment on Patient-Reported Outcomes Among Patients With Hepatitis Delta in Europe [Poster FRI-605]. Paper presented at: European Association for the Study of the Liver (EASL) Congress 2026; 27-30 May, 2026; Barcelona, Spain.
6. Wedemeyer H, Aleman S, Brunetto M, et al. Efficacy and safety at 96 weeks of bulevirtide 2 mg or 10 mg monotherapy for chronic hepatitis D (CHD): results from an interim analysis of a phase 3 randomized study. [Abstract]. Paper presented at: European Association for the Study of the Liver (EASL); June 21-24, 2023; Vienna, Austria.
7. Wedemeyer H, Aleman S, Brunetto MR, et al. A Phase 3, Randomized Trial of Bulevirtide in Chronic Hepatitis D. *N Engl J Med.* 2023;389(1):22-32.
8. Wedemeyer H, Aleman S, Andreone P, et al. Bulevirtide Monotherapy at Low and High Doses in Patients With Chronic Hepatitis Delta: 24-Week Interim Data of the Phase 3 MYR301 Study [Poster 2730]. Paper presented at: European Association for the Study of the Liver (EASL): The Digital International Liver Congress; 23-26 June, 2021.

9. ClinicalTrials.gov. Study to Assess Efficacy and Safety of Bulevirtide in Participants With Chronic Hepatitis Delta (CHD). ClinicalTrials.gov Identifier: NCT03852719. Available at https://clinicaltrials.gov/ct2/show/study/NCT03852719. Accessed: June 2026. Last Updated: 22 August 2025.

Abbreviations

BLV=bulevirtide-gmod
CPT=Child-Pugh-Turcotte
EQ-5D-5L=Five-Level
FSS=Fatigue Severity Scale
HBQOL=Hepatitis B Quality of Life
HQLQ=Hepatitis Quality of Life Questionnaire
LLOD=lower limit of detection
LSM=least squares mean
OR=odds ratio
PRO=patient-reported outcome
SF-36=36-item Short Form Health Survey
SUBQ=subcutaneous(ly)
TD=treatment difference
VAS=visual analog scale
WPAI=Work Productivity and Activity Impairment

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Hepcludex US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/hdv/hepcludex/hepcludex_pi.

Follow-Up

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