GILEAD | Medical Information

Hepcludex® (bulevirtide-gmod) Use in Patients >65 Years of Age

This document is in response to your request for information regarding the use of Hepcludex® (bulevirtide-gmod [BLV]) for the treatment of chronic HDV infection in patients >65 years of age.

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.

Product Labeling[1]

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).

Clinical trials of BLV did not include participants aged 65 years and over to determine whether they respond differently from younger participants.

The pharmacokinetics of BLV have not been evaluated in elderly participants with HDV infection (65 years of age and older).

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 BLV Use in Participants ≥65 Years

In phase 2/2b clinical studies (MYR202, MYR203, and MYR204) and a phase 3 study (MYR301), participants aged ≥65 years were not eligible for study enrollment.[2-5] No studies have been conducted in participants aged ≥65 years.

Real-World Data on BLV Use in Patients ≥65 Years

Case Report

There are limitations in the interpretation of case reports. Case reports cannot be generalized. Unlike controlled clinical trials, causality cannot be inferred based on uncontrolled observational data. Additionally, incidence or prevalence cannot be estimated due to the lack of a representative population sample. Other limitations of case reports include the retrospective design and publication bias.[6]

Italian compassionate use program

Loglia et al presented details of a 69-year-old, female, White patient with HBeAg-negative status and HDV-related compensated cirrhosis (Table 1). She was a non-responder to previous PEG-IFNα therapy and further use of PEG-IFN was contraindicated due to portal HTN (splenomegaly and thrombocytopenia). The patient was started on BLV 10 mg/day (self-administered as two SUBQ injections [two 5-mg vials]) as part of a compassionate use program prior to the EMA conditional approval of BLV 2 mg. The patient also received ongoing treatment with TDF.[7]

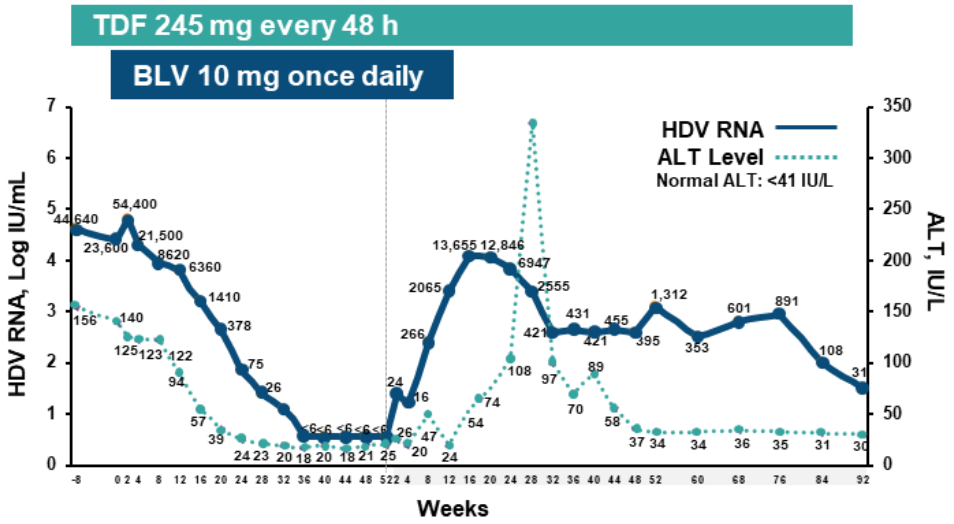
BLV treatment was withdrawn at Week 52 following the diagnosis of an endometrial carcinoma. ALT levels rapidly normalized, and HDV RNA levels became undetectable during BLV treatment. After the discontinuation of BLV, HDV RNA levels and ALT levels increased (peak at Week 28: 333 IU/L), and both markers decreased within the normal range by Week 48 off-therapy (Figure 1). HDV reactivation was not associated with any sign of clinical decompensation. At Week 96 off-therapy, HBsAg and HDV RNA levels were low, and ALT levels were normal.[7]

Table 1. Italian Compassionate Use Program: Patient Characteristics and Treatment Outcomes[7]

Patient Demographics and PMH	HDV/HBV Treatments	Variables	Notes
• 69 y/o, female, White • Compensated cirrhosis (CPT A5), no HCC or esophageal varices • HDV GT 1, HBV GT D • Diabetes mellitus (diet therapy), osteopenia, mild arterial HTN, uterine polyps	• Previous non-responder to PEG-IFNα and later contraindicated to repeat IFN due to portal HTN (thrombocytopenia and splenomegaly) • BLV 10 mg once daily × 52 wk • TDF 245 mg every 48 h before BLV and continued after withdrawal of BLV	**Baseline:** • ALT: 140 U/L • AST: 83 U/L • Platelet: 95 × 10^9/L • Liver stiffness: 17.3 kPa • Cr: 1.06 mg/dL • Esophageal varices: none **Week 48:** • ALT: 21 U/L • AST: 22 U/L • Platelet: 115 × 10^9/L • Liver stiffness: 21 kPa • Cr: 0.94 mg/dL • Esophageal varices: not assessed	• IgG levels normalized • HBsAg levels significantly decreased after BLV was discontinued

Abbreviations: CPT=Child-Pugh-Turcotte; GT=genotype; HCC=hepatocellular carcinoma; PMH=past medical history; y/o=years old.

Figure 1. Italian Compassionate Use Program: Treatment Course and Virological and Biochemical Variables[7]



Bile acids increased significantly during BLV treatment and rapidly normalized after the discontinuation of BLV. The asymptomatic increase of serum bile acid levels >160 mcmol/L was observed at Weeks 20 and 24 and was likely due to BLV being self-administered before blood sampling and not after, as is usually done. No significant increases in HDV- or HBV-specific IFN-γ T-cell responses were observed during BLV treatment or during virological relapse.[8]

References

1. Enclosed. Gilead Sciences Inc. HEPCLUDEX® (bulevirtide-gmod) injection, for subcutaneous use. US Prescribing Information. Foster City, CA.
2. Wedemeyer H, Schoneweis K, Bogomolov P, et al. Safety and efficacy of bulevirtide in combination with tenofovir disoproxil fumarate in patients with hepatitis B virus and hepatitis D virus coinfection (MYR202): a multicentre, randomised, parallel-group, open-label, phase 2 trial. *Lancet Infect Dis.* 2022.
3. 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.
4. Asselah T, Chulanov V, Lampertico P, et al. Bulevirtide Combined with Pegylated Interferon for Chronic Hepatitis D. *N Engl J Med.* 2024;391(2):133-143.
5. Lampertico P, Bogomolov PO, Chulanov V, et al. Phase 2 Randomised Study of Bulevirtide as Monotherapy or Combined With Peg-IFNalpha-2a as Treatment for Chronic Hepatitis Delta. *Liver Int.* 2025;45(2):e70008.
6. Nissen T, Wynn R. The Clinical Case Report: A Review of Its Merits and Limitations. *BMC Res Notes.* 2014;7:264. https://www.ncbi.nlm.nih.gov/pubmed/24758689
7. Loglio A, Ferenci P, Renteria SCU, et al. Excellent virological and clinical responses maintained over 3 years of continuous Bulevirtide treatment in patients with HDV compensated cirrhosis and clinically significant portal hypertension [Poster 1448]. Paper presented at: European Association for the Study of the Liver (EASL): The Digital International Liver Congress; 23-26 June, 2021.
8. Loglio A, Ferenci P, Renteria SCU, et al. Safety and effectiveness of up to 3 years' bulevirtide monotherapy in patients with HDV-related cirrhosis. *Journal of Hepatology.* 2022;76(2):464-469.

Abbreviations

BLV=bulevirtide-gmod
HBeAg=hepatitis B envelope antigen
HBsAg=hepatitis B surface antigen
HTN=hypertension
IFN=interferon
PEG-IFNα=pegylated interferon α
SUBQ=subcutaneous(ly)
TDF=tenofovir disoproxil fumarate

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

For any additional questions, please contact Gilead Medical Information at:

☎1-866-MEDI-GSI (1-866-633-4474) or www.askgileadmedical.com

Adverse Event Reporting

Please report all adverse events to:

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FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or www.accessdata.fda.gov/scripts/medwatch

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