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Livdelzi® (seladelpar) Switching From Fibrates

This document is in response to your request for information regarding switching from fibrates to Livdelzi® (seladelpar [SEL]) for the treatment of primary biliary cholangitis (PBC).

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Summary

Clinical Studies on Switching From Fibrates to SEL

In a phase 3 study and its ongoing, open-label extension, prior use of fibrates did not impact the biochemical response to SEL compared with placebo through 12 months of treatment.[1,2]

- Regardless of prior fibrate use, composite biochemical response was sustained through 18 months of treatment in participants who received SEL and improved in participants who switched from placebo to SEL at Month 12.[3]
- The incidence of overall AEs and liver-related AEs were similar between participants with and without prior fibrates and/or OCA use.[3]

Real-World Data on Switching From Fibrates to SEL

A retrospective, observational study using data from the ColHai registry in Spain assessed the effectiveness outcomes of patients who switched to SEL from UDCA + BZF (n=56) or from UDCA + OCA + BZF (n=97).[3]

- POISE response and ALP normalization at 6 months was achieved in 58% (n/N=11/19) and 21% (n/N=4/19) of patients, respectively, who switched to SEL from UDCA + BZF and in 49% (n/N=27/55) and 20% (n/N=11/55) of patients who switched from UDCA + OCA + BZF.
- Among all patients who received SEL (n=320), any-grade AEs were reported in 82 patients (25.6%); the most frequently reported AEs (≥5%) were abdominal pain (n=29 [9.1%]), transaminase elevation, (n=25 [7.8%]), and headache (n=16 [5%]).

Clinical Studies on Switching From Fibrates to SEL

Currently, there is no specific guidance on switching from fibrates to SEL.

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RESPONSE and ASSURE Studies

Study design and demographics

RESPONSE was a phase 3, international, randomized, placebo-controlled study that evaluated SEL 10 mg in participants with PBC and an inadequate response to or intolerance of first-line treatment with UDCA (N=193). Participants were randomly assigned (2:1) to receive either SEL 10 mg (n=128) or placebo (n=65) once daily for 12 months.[1] The use of fibrates before screening was an exclusion criterion, and a washout period of 6 weeks was required prior to enrollment.[4] At completion of the RESPONSE study, participants were eligible to enroll in the ongoing phase 3, long-term, open-label study, ASSURE, in which participants either continued treatment with SEL 10 mg (n=104) or switched from placebo to SEL 10 mg (n=54).[3]

For RESPONSE, the primary composite endpoint was the proportion of participants at Month 12 who achieved a biochemical response, which was defined as an ALP level <1.67 × ULN, an ALP level decrease by ≥15%, and a TB level ≤1 × ULN. Key secondary endpoints included ALP normalization (≤1 × ULN) at Month 12 and change from BL to Month 6 in weekly mean pruritus NRS scores among participants with an NRS score ≥4 (eg, moderate-to-severe pruritus) at BL.[1]

For RESPONSE, pruritus intensity, assessed using pruritus NRS data, were collected daily via the use of an electronic diary during the run-in period and through Month 6, then collected for 7 consecutive days each month through to the end of the treatment period.[4]

In the SEL 10 mg and placebo groups, fibrates were previously used in 5.5% (n=7) and 7.7% of participants (n=5), respectively, and fibrates and/or OCA were previously used in 15.6% (n=20) and 20% of participants (n=13), respectively.[4] Of the 33 participants who had prior fibrate and/or OCA use in the RESPONSE study, 27 enrolled in the ASSURE study. An analysis evaluated outcomes among the participants from RESPONSE who continued in the ASSURE study according to prior OCA and/or fibrates use.[3]

Table 1. RESPONSE: BL Demographics and Disease Characteristics According to Prior OCA and/or Fibrates Use[3]

Key Demographics and Characteristics	Prior Treatment With Fibrates/OCA		No Prior Treatment With Fibrates/OCA	
	SEL 10 mg (n=20)	Placebo (n=13)	SEL 10 mg (n=108)	Placebo (n=52)
Age, mean ± SD, years	55.8±9.3	55.4±11.1	56.7±10.2	57.4±8.7
Female, n (%)	18 (90)	12 (92)	105 (97)	48 (92)
Duration of PBC, mean ± SD, years	9.5±6.3	12.3±7.9	7.9±6.8	7.7±5.8
Prior use of fibrates, n (%)	7 (35)	5 (38)	–	–
Duration of fibrate/OCA treatment, mean ± SD, years	2.7±2.4	2±1.4	–	–
Duration of fibrate/OCA washout prior to study, mean ± SD, years	0.9±0.8	0.8±0.8	–	–
Cirrhosis at BL,[a] n (%)	2 (10)	0	16 (15)	9 (17)
ALP, mean ± SD, U/L	371±145	348.6±141.9	304.1±116.2	305.1±110.7
TB, mean ± SD, mg/dL	0.8±0.2	0.6±0.2	0.8±0.3	0.8±0.3

[a]All participants with cirrhosis at BL were Child-Pugh Class A.

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Efficacy

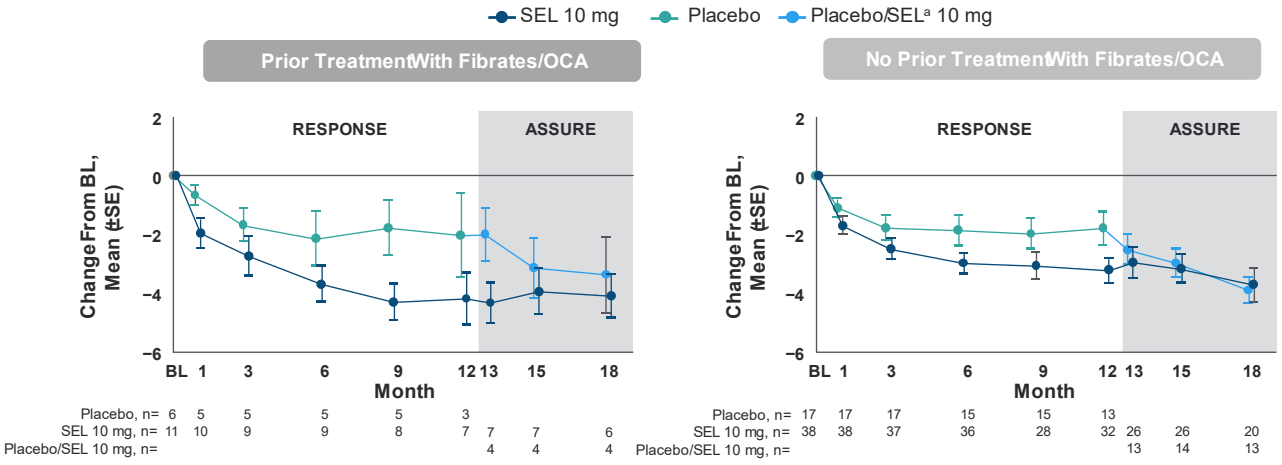
The primary composite endpoint for RESPONSE was achieved by more participants in the SEL arm than in the placebo arm (responder rate [95% CI]: 61.7% [53.3–70.1%] vs 20% [10.3–29.7%], respectively).[1] Prior use of fibrates did not impact the response to SEL compared with placebo in regard to the primary endpoint (Table 2) or the key secondary endpoint of change from BL to Month 6 in weekly pruritus NRS scores among participants with a pruritus NRS score ≥4 at BL (Figure 1).[1,2] Fewer participants with prior fibrates and/or OCA use than those with no prior use achieved the key secondary endpoint of ALP normalization at Month 12 (Table 2), although the ALP percent change from BL was similar. Declines in ALT and GGT were similar between the participants with and without prior fibrates and/or OCA use, and the TB percent change was generally stable.[3]

Table 2. RESPONSE and ASSURE: Composite Biochemical Response and ALP Normalization According to Prior OCA and/or Fibrates Use[3]

Outcome, n/N (%)		Month 12 (RESPONSE)		Month 18 (ASSURE)	
		SEL 10 mg	Placebo	SEL 10 mg	Placebo/SEL[b]
Composite biochemical response[a]	Prior treatment with fibrates/OCA	9/20 (45)	1/13 (8)	9/15 (60)	7/11 (64)
	No prior treatment with fibrates/OCA	70/108 (65)	12/52 (23)	54/87(62)	32/41 (78)
ALP normalization	Prior treatment with fibrates/OCA	2/20 (10)	0/13 (0)	2/15 (13)	1/11 (9)
	No prior treatment with fibrates/OCA	30/108 (28)	0/52 (0)	32/87(37)	13/41 (32)

[a]Defined as an ALP level <1.67 × ULN, an ALP level decrease by ≥15%, and a TB level ≤1 × ULN.
[b]Included participants who received placebo in RESPONSE and were switched to SEL 10 mg at ASSURE enrollment.

Figure 1. RESPONSE and ASSURE: Change in Pruritus NRS Score Among Participants With BL Pruritus NRS Score ≥4 According to Prior OCA and/or Fibrates Use[3]



[a]Includes participants who received placebo in RESPONSE and were switched to SEL 10 mg at ASSURE enrollment.

Safety[3]

Incidences of overall AEs and liver-related AEs were similar between participants with and without prior fibrates and/or OCA use (Table 3). The occurrence of ALT or AST >3 × ULN was similar between the SEL and placebo groups in both RESPONSE (SEL: prior fibrates/OCA,

20% [4/20]; no prior fibrates/OCA, 5% [5/108]; placebo: prior fibrates/OCA, 15% [2/13]; no prior fibrates/OCA, 10% [5/52]) and ASSURE (SEL: prior fibrates/OCA, 6% [1/16]; no prior fibrates/OCA, 1% [1/88]; placebo/SEL: 0). No drug-related SAEs or AEs that led to death were reported.

Table 3. RESPONSE and ASSURE: Safety Overview According to Prior OCA and/or Fibrates Use[3]

AEs, n (%)		Prior Treatment With Fibrates/OCA		No Prior Treatment With Fibrates/OCA	
RESPONSE Study (Month 12)		**SEL 10 mg (n=20)**	**Placebo (n=13)**	**SEL 10 mg (n=108)**	**Placebo (n=52)**
Any AE		17 (85)	11 (85)	94 (87)	44 (85)
Grade ≥3 AEs		1 (5)	1 (8)	13 (12)	4 (8)
SAEs		1 (5)	1 (8)	8 (7)	3 (6)
AEs that led to treatment withdrawal		1 (5)	1 (8)	3 (3)	2 (4)
AEs that led to study discontinuation		1 (5)	1 (8)	2 (2)	2 (4)
Liver-related AEs		2 (10)	1 (8)	6 (6)	5 (10)
Most frequently reported AEs (occurred in >10% of participants in any group)	COVID-19	8 (40)	3 (23)	15 (14)	7 (13)
	Pruritus	2 (10)	2 (15)	4 (4)	8 (15)
	Asthenia	0	3 (23)	5 (5)	1 (2)
	Arthralgia	0	2 (15)	8 (7)	2 (4)
	Nasopharyngitis	0	2 (15)	7 (6)	3 (6)
	Hypercholesterolemia	0	2 (15)	1 (1)	0
	Gastroenteritis	0	2 (15)	0	1 (2)
ASSURE Open-Label Extension (Month 12 through Month 18)		**SEL 10 mg (n=16)**	**Placebo/SEL[a] (n=11)**	**SEL 10 mg (n=88)**	**Placebo/SEL[a] (n=43)**
Any AE		12 (75)	8 (73)	59 (67)	31 (72)
Grade ≥3 AEs		2 (13)	1 (9)	6 (7)	2 (5)
SAEs		2 (13)	1 (9)	3 (3)	4 (9)
AEs that led to treatment withdrawal		1 (6)	0	0	0
AEs that led to study discontinuation		0	0	0	0
Liver-related AEs		2 (13)	0	3 (3)	0
Most frequently reported AEs (occurred in >10% of participants in any group)	Pruritus	2 (13)	0	7 (8)	0
	Anemia	2 (13)	0	2 (2)	2 (5)
	Herpes zoster	2 (13)	0	2 (2)	0
	Headache	1 (6)	0	1 (1)	5 (12)
	Diarrhea	0	2 (18)	1 (1)	3 (7)
	Hematuria	0	2 (18)	0	0

[a]Included participants who received placebo in RESPONSE and were switched to SEL 10 mg at ASSURE enrollment.

Real-World Data on Switching From Fibrates to SEL

Retrospective, Multicenter, Observational Study[3]

Study design and demographics

A retrospective, multicenter, observational study in Spain assessed the effectiveness of SEL in patients from the ColHai registry who switched to SEL from UDCA + BZF (n=56) or UDCA + OCA + BZF (n=97). Endpoints included POISE response and ALP normalization,

and symptoms of pruritus and fatigue were assessed categorically. BL characteristics are summarized in Table 4.

Table 4. BL Demographics and Disease Characteristics (Diaz-Gonzalez et al)[3]

Key Demographics and Characteristics	UDCA + BZF→SEL (n=56)	UDCA + OCA + BZF→SEL (n=97)
Age, median (IQR), years	58 (49.3–64.5)	60 (51–66.9)
Female, n (%)	54 (96.4)	87 (89.7)
Liver stiffness, median (IQR), kPa	7.9 (5.1–14.3)	7.4 (6–11.3)
Cirrhosis, n (%)	13 (23.2)	18 (18.6)
AST × ULN, median (IQR)	1.5 (1–2.2)	1.1 (0.8–1.7)
ALT × ULN, median (IQR)	1.3 (0.8–2.3)	0.8 (0.6–1.3)
ALP × ULN, median (IQR)	1.7 (1.3–2.6)	1.2 (0.9–1.7)
GGT × ULN, median (IQR)	4.7 (1.8–9.3)	1.7 (0.8–5.9)
TB, median (IQR), mg/dL	0.7 (0.4–1.1)	0.6 (0.4–1)
Pruritus, n (%)	24 (42.9)	32 (33)
Fatigue, n (%)	22 (41.5)	32 (33)
BL POISE response, n (%)	21 (38.2)	65 (68.4)
BL Paris 2 response, n (%)	11 (20)	45 (47.4)

Efficacy

The effectiveness outcomes of SEL treatment from BL through 6 months are presented in Table 5.

Table 5. Effectiveness of Switching From OCA or BZF to SEL Through 6 Months (Diaz-Gonzalez et al) [3]

Parameter		UDCA + BZF→SEL	UDCA + OCA + BZF →SEL
POISE response, n/N (%)	BL	21/55 (38)	65/95 (68)
	1 month	22/39 (56)	43/72 (60)
	3 months	17/39 (44)	44/78 (56)
	6 months	11/19 (58)	27/55 (49)
ALP normalization, n/N (%)	BL	9/56 (16)	32/95 (34)
	1 month	10/39 (26)	19/73 (26)
	3 months	5/39 (13)	16/78 (21)
	6 months	4/19 (21)	11/55 (20)
Loss of POISE response, %		Not reported	29.2
Loss of Paris 2 response, %		Not reported	37.8

Among those who switched to SEL, improvements in fatigue and pruritus were reported in 38.3% and 81.6% of patients, respectively.

Safety

Among all patients who received SEL (n=320), any-grade AEs were reported in 82 patients (25.6%); the most frequently reported AEs (≥5%) were abdominal pain (n=29 [9.1%]), transaminase elevation (n=25 [7.8%]), and headache (n=16 [5%]). Twenty-two patients (6.9%) discontinued SEL due to AEs.

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References

1. Hirschfield GM, Bowlus CL, Mayo MJ, et al. A Phase 3 Trial of Seladelpar in Primary Biliary Cholangitis. *N Engl J Med.* 2024;390(9):783-794.
2. Villamil A, Pratt D, Kremer AE, et al. Efficacy and Safety of Seladelpar in Patients With Primary Biliary Cholangitis Previously Treated With Fibrates or Obeticholic Acid. [Poster #THU-274]. Paper presented at: European Association for the Study of the LiveR; May 7–10 2025; Amsterdam, the Netherlands.
3. Diaz-Gonzalez A, Monton C, Brosell M, et al. Management of patients with primary biliary cholangitis in the post-obeticholic era: real-world effectiveness data on elafibranor and seladelpar from the ColHai registry [Presentation]. Paper presented at: European Association for the Study of the Liver (EASL); May 27-30, 2026; Barcelona, Spain.
4. Hirschfield GM, Bowlus CL, Mayo MJ, et al. A Phase 3 Trial of Seladelpar in Primary Biliary Cholangitis.[Supplementary Appendix]. *N Engl J Med.* 2024;390(9):783-794.

Abbreviations

AE=adverse event
ALP=alkaline phosphatase
BL=baseline
BZF=bezafibrate
GGT=γ-glutamyl transferase
NRS=numerical rating scale
OCA=obeticholic acid
PBC=primary biliary cholangitis
POISE=PBC OCA International Study of Efficacy
SAE=serious adverse event
SEL=seladelpar
TB=total bilirubin
UDCA=ursodeoxycholic acid
ULN=upper limit of normal

Product Label

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

Follow-Up

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

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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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