IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

IN RE: GLUGAGON-LIKE PEPTIDE-1 RECEPTOR AGONISTS (GLP-1 RAS) PRODUCTS LIABILITY LITIGATION	:	**CIVIL ACTION**
	:	**MDL No. 3094**
	:	**24-md-3094**
THIS DOCUMENT RELATES TO:	:	
	:	**HON. KAREN SPENCER MARSTON**
ALL ACTIONS/ALL CASES	:	

CASE MANAGEMENT ORDER NO. 18

CROSS CUTTING ISSUES

AND NOW, this 23rd day of August, 2024, upon consideration of Defendants' letter brief concerning early discovery and motion practice on three "cross cutting" issues (Doc. No. 174), Plaintiffs' letter brief concerning the same (Doc. No. 175), and the arguments made by counsel during status conferences on July 10, July 26, and August 2, 2024, the Court finds as follows:

1. This MDL involves personal injury actions stemming from the use of glucagon-like peptide-1 (GLP-1) receptor agonists and GLP-1/glucose-dependent insulinotropic polypeptide (GIP) dual receptor agonists (collectively, "GLP-1 RAs") manufactured by Defendants and sold under the brand names Ozempic, Wegovy, Rybelsus, Trulicity, and Mounjaro.[1] (Doc. No. 1.) Currently, there are 842 cases included in the MDL, but Plaintiffs' leadership counsel have suggested that this number will easily reach the thousands, if not tens of

[1] Ozempic, Wegovy, and Rybelsus are manufactured by the Novo Nordisk Defendants, and Trulicity and Mounjaro are manufactured by Defendant Eli Lilly and Company. Cases involving a sixth GLP-1 RA, named Saxenda, are also being considered by the Judicial Panel on Multidistrict Litigation (JPML) for inclusion in the MDL. (*See* Doc. No. 201.)

thousands. (*See* June 10, 2024 Hr'g. Tr. at 16:18–23 ("And there are known to us, meaning co-lead counsel, approximately 5,000 Novo-only cases under investigation; about 1,200 Lilly-only cases; and then about 1,400 combined Novo and Lilly.").)

2. Although the alleged drug, dosage, and precise injury vary by Plaintiff, there are many commonalities. Notably, each Plaintiff claims they were prescribed one or more of the five identified drugs for the treatment of type 2 diabetes and/or long-term weight management and that as a result, they suffered gastrointestinal symptoms and/or injuries, such as gastroparesis, ileus/intestinal obstruction, cholecystitis, and severe nausea and vomiting.[2]

3. The parties have proposed two competing schedules for structuring discovery and other pre-trial proceedings. Defendants argue that the Court should "prioritize the resolution of three pivotal questions," which they refer to as "cross cutting" issues: (1) gastroparesis diagnostic testing, (2) preemption and warnings, and (3) general causation. (Doc. No. 174.) Plaintiffs oppose any bifurcation of discovery and argue that the Court should instead select six bellwether cases and allow general and case-specific discovery to proceed simultaneously as to those Plaintiffs. (Doc. No. 175.) The Court agrees with Defendants as to the first two issues and reserves ruling on the third.[3]

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[2] The Court has stayed two individual cases in which the Plaintiffs allegedly suffered veinous thromboembolisms after using one of the identified GLP-1 RAs. (*See* Doc. No. 207.) The parties are currently seeking permission from the JPML to include these and similar cases in this MDL. At this time, however, the MDL is limited to cases alleging gastrointestinal events. (*See* Doc. No. 1 at 2.)

[3] Numerous other courts overseeing MDLs have found it effective to prioritize discovery and motion practice on specific issues as a means to efficiently manage and streamline pretrial proceedings. *See, e.g.*, *In re Zantac (Ranitidine) Prods. Liab. Litig.*, MDL No. 20-MD-2924, Pretrial Order No. 30 (S.D. Fla. June 18, 2020) (establishing a case management schedule in a pharmaceutical MDL that prioritizes discovery and motion practice on the issue of general causation); *In re: Viagara (Sildenafil Citrate) Prods. Liab. Litig.*, Case No. 3:16-md-02691-RS, Doc. No. 102 (N.D. Cal. Sept. 26, 2016) (limiting initial discovery in pharmaceutical MDL to the issue of general causation); *In re: Incretin Mimetics Prods. Liab. Litig.*, MDL Case No. 13md2425 AJB (MDD), Doc. No. 325 (S.D. Cal. Feb. 18, 2014) (limiting initial discovery and document production in pharmaceutical MDL to issue of general causation); *id.* at Doc. No. 744 (expanding scope of prior scheduling order to also include early discovery

Issue 1: Gastroparesis Diagnostic Testing

4. As to the first issue, the Court finds that early motion practice on how to reliably diagnose gastroparesis will be a pivotal issue in this action. Plaintiffs' leadership counsel have represented that they anticipate the "vast majority, over 95%" of the cases eventually filed as part of this MDL will allege that the individual Plaintiffs suffered gastroparesis. (June 10, 2024 Hr'g. Tr. at 17:23–25.) Defendants argue—and claim their experts will attest—that to reliably diagnose a patient with gastroparesis the clinician would have to have performed objective testing, such as a gastric emptying study (GES), at the time symptoms presented. (Doc. No. 174 at 2–4; July 10, 2024 Hr'g. Tr. at 74:5–20, 90:2–6.) Yet, many of the Plaintiffs claiming to have suffered from gastroparesis have not alleged contemporaneous objective testing occurred. (*See* July 10, 2024 Hr'g. Tr. at 73:4–13.) Accordingly, Defendants argue it is worthwhile for the parties, and the Court, to know at the beginning of this litigation whether gastroparesis may be reliably diagnosed in a clinical setting absent objective testing, because if not, it could severely limit the number and nature of the claims presented.[4] (*See* Doc. No. 174 at 2–4.)

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and motion practice on the issue of preemption); *cf.* Manual for Complex Litigation, Fourth at § 22.634 (encouraging "the judge and counsel" to "work to narrow the issues, claims, and defenses" early in the case and to identify "[i]ssues to be taken up early in the litigation," such as "whether the facts and expert evidence support a finding that the products or acts in question have the capacity to cause the type of injuries alleged," and whether the "plaintiffs' claims are barred"); Douglas G. Smith, *Resolution of Common Questions in MDL Proceedings*, 66 Kan. L. Rev. 219, 253 (2017) ("[I]n many MDL proceedings there are generic issues that may be dispositive of the entire litigation, and resolution of such issues early in the proceedings may render further proceedings unnecessary. Frontloading consideration of such issues has obvious efficiencies for the litigation. . . . Indeed, even where the court ultimately denies motions seeking to narrow the litigation, such proceedings may play a valuable role in educating the court regarding the common issues in the case at the outset.").

[4] Plaintiffs counter that a GES is not required for a reliable diagnosis and claim their experts will attest that there are other reliable methods for diagnosing an individual with gastroparesis. (*See, e.g.*, June 10, 2024 Hr'g. Tr. at 17:18–24 (arguing that there "are several other ways that gastroparesis can be diagnosed" and noting that "a review of these cases by experts will reveal a clinical diagnosis of gastroparesis"). But that is precisely the issue to be decided, not an argument in favor of waiting to decide it.

5. Plaintiffs argue that they need only allege and ultimately, prove an *injury*, not a particular *diagnosis*, so it is inefficient to prioritize expert discovery on this issue early in the case. (*See* July 10, 2024 Hr'g. Tr. at 59:22–60:3.) That argument, although technically correct, misunderstands the importance of proving gastroparesis specifically, as opposed to gastrointestinal symptoms generally, in this litigation. As the Court discusses below in connection with Issue 2, the learned intermediary doctrine could pose a major hurdle to Plaintiffs. The GLP-1 RAs included in this MDL were approved by the FDA for use in accordance with their respective labels. Most of those labels warned for gastrointestinal symptoms, including nausea and vomiting, and to the extent a symptom or illness was adequately warned for on the label, many Plaintiffs may find their failure to warn claims fail under the learned intermediary and similar doctrines. *See, e.g.*, *Zitney v. Wyeth LLC*, 243 A.3d 241, 246 (Pa. Super. Ct. 2020) (applying Pennsylvania's learned intermediary doctrine and finding that "because Appellants conceded that Appellees fulfilled their duty to provide content-appropriate warning labels in their metoclopramide packaging, the trial court properly found that Appellees had not breached their duty to [warn] Appellants. Accordingly, Appellees were entitled to judgment as a matter of law and the trial court, therefore, did not err in entering summary judgment in favor of Appellees"). Not all the GLP-1 RAs' labels, however, warned for *gastroparesis*, which is, again, the primary injury alleged in this MDL.

6. Given the proportion of Plaintiffs alleging gastroparesis and the potential importance of that diagnosis to Plaintiffs' failure to warn claims, the Court finds this issue is cross cutting and an early decision on how to reliably diagnose that condition is appropriate. Accordingly, the Court grants Defendants' request for early motion practice as to Issue 1 and directs the parties to meet and confer so that they are prepared to jointly propose deadlines for

the exchange of expert reports, the taking of expert depositions, and the filing of Rule 702 motions at the status conference on September 16, 2024.

Issue 2: Preemption and Adequacy of Warning Labels

7. Second, Defendants request early discovery and motion practice on whether "Plaintiffs' claims are preempted by federal law and/or fail because the warnings included in the product labeling—which the Food and Drug Administration ('FDA') has repeatedly reviewed and approved after scrutinizing available scientific data—are adequate as a matter of law." (Doc. No. 174 at 1.) As mentioned above, all parties agree that the GLP-1 RAs included in this MDL were approved by the FDA for use in accordance with their respective labels, which included some warnings of gastrointestinal side effects.

8. "The FDA regulates the safety information that appears on the labels of prescription drugs that are marketed in the United States." *Merck Sharp & Dohme Corp.*, 587 U.S. at 303 (citing 21 U.S.C. § 355(b)(1)(F) and 21 C.F.R. § 201.57(A) (2018)).[5] As such, drug manufacturers work with the FDA to develop an appropriate label for their brand-name prescription drugs. *Id.* at 304. "But FDA regulations also acknowledge that information about drug safety may change over time, and that new information may require changes to the drug label." *Id.* Although manufacturers typically "seek advance permission from the FDA to make substantive changes to their drug labels," one FDA regulation, "called the 'changes being effected' or 'CBE' regulation[,] permits drug manufacturers to change a label without prior

[5] Among other things FDA regulations require drug labels to include: "(1) prominent 'boxed warnings about risks that may lead to death or serious injury; (2) contraindications describing any situation in which the drug should not be used because the risk of use outweighs any therapeutic benefit; (3) warnings and precautions about other potential safety hazards; and (4) any adverse reactions for which there is some basis to believe a causal relationship exists between the drug and the occurrence of the adverse event." *Id.* at 304 (citing 21 C.F.R. 201.57(c)).

FDA approval if the change is designed to 'add or strengthen a warning' where there is 'newly acquired information' about the 'evidence of a causal association' between the drug and a risk of harm." *Id.* at 304–05 (quoting 21 C.F.R. § 314.70(c)(6)(iii)(A)).

9. In the context of brand-name prescription drugs, these federal regulations will preempt state laws requiring additional warnings if the manufacturer can show it would have been impossible to comply with both the federal regulations and state law regarding adequate warnings. *See id.* at 314 ("The underlying question for this type of impossibility pre-emption defense is whether federal law (including appropriate FDA actions) prohibited the drug manufacturer from adding any and all warnings to the drug label that would satisfy state law."). Specifically, when the manufacturer provides "'clear evidence' that the FDA would not have approved a change to [a prescription] drug's label," federal law preempts state law claims grounded in the assertion "that drug manufacturer failed to warn consumers of the change-related risks associated with using the drug." *Id.* at 302–03 (referencing the holding of *Wyeth v. Levine*, 555 U.S. 555, 571 (2009)). "'[C]lear evidence' is evidence that shows the court that the drug manufacturer fully informed the FDA of the justifications for the warning required by state law and that the FDA, in turn, informed the drug manufacturer that the FDA would not approve a change to the drug's label to include that warning." *Id.* at 303.

10. The question of whether a prescription drug label adequately disclosed the relevant risks is an issue of fact that may ultimately need to be decided by a jury. *See, e.g.*, *In re Avandia Mktg., Sales Practices & Prods. Liab. Litig.*, 817 F. Supp. 2d 535, 537 (E.D. Pa. 2011) ("Because the [Plaintiffs' Steering Committee] has presented sufficient evidence of labeling omissions regarding CHF risks, including those concerning certain patient subpopulations and sufficient evidence that GSK knew or should have known about those risks well before the

labels disclosed them, as well as evidence of inconsistencies and ambiguities within the 2001 label, the Court finds that a reasonable jury could conclude that the labels were incomplete, inaccurate, or misleading as to CHF risks. Thus, the issue cannot be resolved as a matter of law and summary judgment on the adequacy of the labels is inappropriate."). The question of preemption, however, "is one for a judge to decide." *Merck Sharp & Dohme Corp.*, 587 U.S. at 303.

11. Here, Plaintiffs raise numerous claims related to the adequacy of Defendants' labels:

> Plaintiffs contend that Defendants' labels fall short of the requirements that a drug label's Warnings and Precautions "include a concise summary of the most clinically significant safety concerns from the label that affect decisions about whether to prescribe the drug, recommendations for patient monitoring to ensure safe use of the drug, and measures that can be taken to prevent or mitigate harm." Plaintiffs further contend that the labels at issue here also do not fully "identify the risk, its consequences, and recommendations for the clinician to prevent or mitigate it, as appropriate". Instead, the labels' reference to common reactions like nausea, vomiting and abdominal pain does not inform prescribers that these symptoms may be signs of life-threatening digestive dysfunction necessitating critical medical care. The labels downplay the symptoms by stating that "the majority of reports of nausea [and] vomiting … decreased over time," minimizing these symptoms and denying prescribers and patients the opportunity to make an informed decision. Lilly's warning about "gastrointestinal adverse reactions, sometimes severe" is likewise inadequate and vague: warning of an episode of severe vomiting does not, itself, warn of the risk of weeks of vomiting due to stomach paralysis, which may lead to hospitalization or death, and which may not abate after stopping the drug.
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> Similarly, a passing reference to "ileus" in the Post-Marketing Events section of a label (distinct from the Warnings section) does not help prescribers identify, understand, or mitigate the risk. As Defendants acknowledge, the additional reference to ileus was spurred by an FDA-initiated review, but Defendants should not have waited for the FDA to act. Manufacturers—not the FDA—are responsible for the labeling of their drugs at all times, and

> manufacturers may not rely on the FDA to promptly ensure the adequacy of drug labeling. Accordingly, as with a warning for gastroparesis, Defendants could have and should have warned of the risk of ileus in the labeling submitted for initial approval and strengthened the warnings in revised labeling through the CBE process.

(Doc. No. 175 at 13.) Plaintiffs argue that these issues are best tackled after fulsome discovery and in the context of individual Plaintiffs identified for bellwether adjudication. (*Id.*)

12. But the Court does not need to consider each Plaintiff's specific circumstances to determine: (1) whether the Court can rule as a matter of law that Defendants' labels adequately warn for the gastrointestinal symptoms and events common to all Plaintiffs (i.e., label adequacy), and (2) whether Defendants should have (or could have) revised their labels to provide additional warnings which Plaintiffs argue were required as a matter of state law (i.e., preemption). Instead, as Plaintiffs acknowledge, to answer those questions the Court will need to "know the drug at issue in the case, the warning label at issue, . . . the alleged deficiencies on the particular warning, what was provided to the FDA, and more importantly what was withheld from the FDA." (*Id.*) The Court will not need to know the specific "injuries claimed by [any individual] Plaintiff," because most Plaintiffs claim the same categories of gastrointestinal

events: gastroparesis, ileus/intestinal obstruction, and severe nausea and vomiting.[6, 7] That is what renders this issue cross cutting. A ruling, for example, that a given label, as a matter of law, adequately warned for gastroparesis or that federal law preempts state law claims to the extent state law would have required the addition of a gastroparesis warning, could limit many of the claims in this MDL or at minimum, hone the parties' arguments as they relate to Defendants' alleged failure to warn.

13. During oral argument on these issues—and after the parties' submitted their letter briefs—Plaintiffs argued for the first time that early discovery and motion practice on Issue 2 is inappropriate because the adequacy of warnings is not just a question of preemption. Plaintiffs assert that, instead, the issue also necessarily involves consideration of the applicability of the learned intermediary doctrine and consideration of the legal effect, if any, of Defendants' unique and substantial campaign to market the GLP-1 RAs directly to consumers. (*See, e.g.*, July 26, 2024 Hr'g. Tr. at 11:13–12:12.) To the extent these issues arise during motion practice on Issue

[6] Plaintiffs argue that "under the case law of this District," the Court must consider the specific warning "that should have been given to a particular plaintiff" when analyzing issues of insufficient warning and preemption. (July 10, 2024 Hr'g. Tr. at 54:24–55:11.) Specifically, Plaintiffs assert that "the case law from this very District in the *Atrium* case, discusses how for determination of warnings, sufficiency of warnings, treating physician information is necessary." (*Id.*) Even if this Court was required to follow the "case law of this District"—and we are not—the *Atrium* case is inapposite. Notably, it involved failure to warn claims in the context of a medical device, not a prescription drug, and the portion of the *Atrium* opinion referenced by Plaintiffs discussed the specificity with which a plaintiff in a medical device case must plead a failure to warn claim, not the evidentiary requirements at summary judgment in a prescription drug case. *See Spear v. Atrium Med. Corp.*, 651 F. Supp. 3d 553, 558 (E.D. Pa. 2022). Moreover, the Court is not asking Plaintiffs to "tender expert reports at the outset of a case" without the "benefit of a factual record." *Id.* Instead, the Court is prioritizing fact discovery and motion practice on this issue. If Plaintiffs believe it is necessary to have testimony from "treating physicians" as to how they interpret Defendants' labels and what additional warnings are "relevant to their decision-making," Plaintiffs are welcome to depose a reasonable number of treating physicians on this issue. *Id.* Indeed, the Court anticipates both sides will put forth expert medical testimony as to the meaning, scope, and adequacy of the warnings included in Defendants' labels.

[7] And to the extent any individual Plaintiff alleges a unique gastrointestinal event requiring individualized evaluation, the Court can and will decide the effect of any overarching ruling as to that specific Plaintiff through a show-cause process.

2—and the Court believes that they will—the Court still finds that the issues are cross cutting and worth deciding at an early stage. Notably, both the viability of the learned intermediary doctrine and the availability of Plaintiffs' direct-to-consumer marketing argument, are legal questions that turn on interpretations of state law and do not require significant discovery beyond what is already being provided in connection with preemption and labeling adequacy mentioned above.[8]

14. Because issues related to the adequacy of each drug's label and the applicability of the preemption doctrine are likely to affect most cases, if not every case, in this MDL, and a ruling on these issues is likely to streamline the litigation, the Court agrees that this is a cross cutting issue worthy of early resolution. Accordingly, the Court grants Defendants' request for early discovery and motion practice as to Issue 2 and directs the parties to meet and confer so that they are prepared to jointly propose deadlines for regulatory and company discovery[9] on

[8] For example, if a state has adopted the learned intermediary or a similar doctrine, then the Court looks only to the label to determine whether the medical provider was adequately warned, and Defendants' marketing campaign may be irrelevant to that analysis. *See, e.g.*, *Zitney*, 243 A.3d at 246 ("Pennsylvania applies the learned intermediary doctrine to claims for failure to warn involving pharmaceutical drugs. Under the learned intermediary doctrine, drug manufacturers must direct required drug-safety warnings to physicians, and not to patients."). Although Plaintiffs argue that the Court will be able to look beyond the label to consider marketing because Defendants marketed these drugs directly to consumers, some states have explicitly rejected an advertising exception to the learned intermediary doctrine. *See Dearinger v. Eli Lilly & Co.*, 510 P.3d 326, 335 (Wa. 2022); *Watts v. Medicis Pharms. Corp.*, 365 P.3d 944, 950–51 (Ariz. 2016); *cf. Centocor, Inc. v. Hamilton*, 372 S.W.3d 140, 161 (Tex. 2012) ("In the more than twelve years since *Perez*, many courts have declined to follow the New Jersey Supreme Court's sweeping departure from the learned intermediary doctrine." (collecting cases)). The Court, however, defers ruling on this legal issue until we consider the parties' briefing on summary judgment as to Issue 2.

[9] As noted above, although Defendants' marketing to a specific Plaintiff or in a specific state may ultimately be relevant discovery once the Court decides these issues and reaches the bellwether stage of discovery, the parties should refrain from pursuing discovery into Defendants' marketing campaigns during early discovery on Issue 2. Such issues are best left until after the Court rules on whether, as a matter of law, any Plaintiff may assert a claim for failure to warn based in whole or in part on a manufacturer's direct-to-consumer marketing.

this issue and for the filing of motions for summary judgment at the status conference on September 16, 2024.

Issue 3: General Causation

15. Last, Defendants request early discovery and motion practice on general causation, i.e., whether the GLP-1 RAs are capable of causing the gastrointestinal events alleged by Plaintiffs. (Doc. No. 174 at 7.) The Court has requested additional briefing on the process for distinguishing causal connection from mere associations attributed to Sir Arthur Bradford Hill, and specifically, how the Hill factors influence the Court's consideration of whether general causation is in fact "cross cutting" or instead, is more appropriately addressed on an individual Plaintiff by individual Plaintiff basis. Accordingly, the Court reserves ruling on Issue 3 until after we review the forthcoming supplemental briefing.

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For the reasons discussed above, it is **ORDERED** that Defendants' request is **GRANTED** as to Issues 1 and 2. The parties shall continue to meet and confer amongst themselves, and if appropriate, with the Special Master, about a proposed scheduling order for discovery and motion deadlines on these issues. The Court will enter a comprehensive scheduling order after considering the parties' joint proposal at the conference on September 16, 2024. The Court defers ruling on whether early discovery and motion practice are appropriate as to Issue 3.

IT IS SO ORDERED.

/s/*Karen Spencer Marston*

KAREN SPENCER MARSTON, J.