GLP-1 Packaging Primer: Perspectives From the Former Chief Scientific Officer of West Pharmaceutical Services

Former Executive | Moderated Call | Moderator: Shane Sullivan | August 29, 2023 | 18 Min Read

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Fran DeGrazio, Former Chief Scientific Officer - West Pharmaceutical Services

KEY QUESTIONS

- How are the major GLP-1 brands packaged? Are there notable differences in preferences between the GLP-1s that are used for diabetes versus those used for obesity?
- What are the nuances of GLP-1s when it comes to the technical specifications of the components?
- What informs pharmaceutical companies' choice of primary packaging vendor? Could you describe the competitive landscape in elastomeric components, containers, and drug delivery devices?
- Do you think that the recent demand for GLP-1s for obesity has come as a surprise to the suppliers in this space? What does capacity look like?
- If you could weigh in on the evolution of the GLP-1 category, including oral GLP-1s, pipeline GLP-1s, and eventual rise of generic GLP-1s, what would you highlight?

HIGHLIGHTS

> On selection criteria for primary packaging and drug delivery devices: "Quality has got to be a given, right? I would say that's you just have to check that off the list. It's also, though, really understanding what customers need, and what they're looking for, and anticipating that. I think that's something that with NovaPure, in particular, was done well at West."
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> On supplier diversity: "The philosophy now has changed through the years, and so, even the FDA through the COVID situation, recommended evaluating secondary sources of supply. Typically, that would mean an 80:20 split. If you were getting 100% of your glass from supplier X, now, you would go to 80% at supplier X and 20% at supplier Y."

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Shane Sullivan: Hello, everyone. Good morning. Thanks for joining us on today's primer concerning GLP-1 packaging.

Before we get started, just one reminder for those in the audience listening in: If you have any questions that you'd like me to relay anonymously to the Advisor on your behalf, feel free to email us at Ask@Guidepoint.com, and I would be glad to do so.

With that, Fran, I'd like to thank you once again for carving out the time today. It should be a really interesting discussion, I think. To begin, would you mind introducing yourself and providing us with an overview of your background, please?

Fran DeGrazio: Sure. I'm Fran DeGrazio. I retired from West Pharmaceutical Services in March of 2022 as the Chief Scientific Officer. I had been at West for close to 39 years in a myriad of technical, and scientific roles, and commercial. Always, on the most part, market-facing and customer-facing roles, so everything from quality, regulatory, I led R&D, I developed their technical customer support group, the analytical contract laboratory business, and so on and so forth. That's my background in a nutshell.

Shane Sullivan: Thank you for the introduction. It sounds particularly relevant to what we'll be discussing today. Let's start out at a high level. How are the major GLP-1 brands packaged? What are the various components, so containers, elastomeric components, drug delivery devices, etc., that are involved?

Fran DeGrazio: Well, right now, there are two major ways, two major packages and ways of delivering. The first is a prefilled syringe system that's inside of an autoinjector. Within the prefilled syringe, of course, you have the glass barrel itself. It's a staked needle syringe, so there's also a rigid needle shield at the end and an elastomeric plunger at the top that would press the drug out. That's filled and placed inside of an autoinjector.

The other way is through a pen system. The pen will have a cartridge that is its primary package, so the glass cartridge is filled. There is a lined seal, what's called a line seal, at the end of this cartridge and a plunger at the other end that again pushes the medicament out. That goes into a pen system. The biggest difference between the two, other than the fact that the primary package, for one, is a syringe system, and for the other, it's a cartridge, you can actually get multiple injections from the pen system. In some cases, depending on the pen, you can dial in a different dosage form.

Shane Sullivan: Thanks for explaining that. Are there notable differences in preferences between the GLP-1s that are used for diabetes versus those used for obesity? Meaning, leaning toward one such system that you

described over the other based on differing administration requirements?

Fran DeGrazio: As far as if you're just talking about is there a preference of an autoinjector versus the pen system, the autoinjector is once-and-done. It's a bit easier to use than the pen system, where the patient would need to replace the needle before every use. There's no difference between those, for instance, if it's for diabetes or if it's for a weight loss situation.

Shane Sullivan: Drugs for either indication could be packaged in either system, in summary?

Fran DeGrazio: That's correct. That's correct.

Shane Sullivan: What are the nuances of GLP-1s when it comes to the technical specifications of the components that you described? For one, you mentioned that they are predominantly packaged in glass from a container standpoint. Are there specific concerns about stability, leachability, or anything else that comes to mind that necessitates the use of maybe the highest-end glass, coated elastomeric components, or other things in that vein?

Fran DeGrazio: Well, GLP-1, it stands for glucagon-like peptide. The pep meaning it's a peptide, which is a smaller size than would be your typical biologic drug, like a monoclonal antibody or something of that nature. Without getting super specific, the use of a coating is really going to be driven probably by other ingredients, and excipients, and things of that nature that may be in the drug solution. Quite often, it's not necessarily always the active ingredient that can cause an incompatibility, it's other ingredients that are added to make the final drug product. That's one consideration there.

The second thing is, in some cases, there may be just, especially because these are high-volume products, the pharma companies that are producing them want to use the highest-quality product they can get to minimize their risk. That's not only risk around an incompatibility situation where a coating or a film would give you benefit, but also things like particles just, in general, or the quality or the consistency of the product and the components themselves. There's other considerations that go into choosing a higher-value elastomeric component, for instance, or a higher-value glass barrel. There's no driver that I know of, at this moment in time at least, around the use of a polymer syringe system to deliver these products.

Shane Sullivan: Moving on, what informs pharmaceutical companies' choice of primary packaging vendor, particularly if they can all meet baseline technical requirements? What have you found to move the needle when it comes to pricing, reputation, regulatory expertise, and the like?

Fran DeGrazio: Well, quality has got to be a given, right? I would say that's you just have to check that off the list. I think what really starts to make a difference are things like the manufacturing network and a global presence, especially for products such as these. When I talk about the manufacturing network, certainly, one of the things I'm talking about is just the capacity and the supply chain considerations, so being able to produce in multiple locations if that's necessary and that type of thing. That certainly is going to have a major implication on choice.

I think another thing is just the technical and regulatory expertise, even around the packaging components themselves, all of these, in the end, go into form whether it be in the pen system or whether it be in the autoinjector, they are part of a combination product from the customer's perspective when we're talking regulatory aspects. There's certainly even more regulatory and technical support needed for those types of products to be able to get them through and approved at the various regulatory authorities. Aside from that, there are always opportunities where technical problems or issues may occur, and so, to be able to have people that have knowledge and experience to be able to jump in and help is also a differentiator.

I think there are maybe things that people don't think about quite as much, such as just the history of relationships with suppliers, even that alone can be very important. There have been, I'm sure, historic times where a supplier may be challenged with a material and there's only limited quantities. If they have a longstanding relationship with you, they're going to work with you more and they understand your business better. There's considerations like that, too, that will go into it.

Shane Sullivan: Could you describe the competitive landscape in GLP-1s when it comes to containers? For context, Stevanato have touted themselves as the leader in pen cartridges. My impression is that Becton, Dickinson or Embecta, maybe you can clarify that, is the market leader when it comes to syringes. Then there's, of course, other manufacturers like Gerresheimer.

Fran DeGrazio: Well, we could start with the cartridges. Yes, Stevanato, I would say, is a leader in the ready-to-use glass cartridge segment of the industry. Where I think Stevanato really started to make a name for themselves years ago was when they realized that the future was ready-to-use already sterilized glass components. Now, at the time, of course, BD, who is the leader in prefillable glass syringe systems, they were supplying the glass, their Hypak system - the Hypak being their brand name for their traditional glass syringe system - to the industry in a pre-sterilized form, so that was ready-to-use.

Other than that segment of the industry, years ago, nothing was being delivered in a sterilized format. That really opened up an opportunity for Stevanato to be able to come out with their EZ-fill line, which really is vials, syringes, and cartridges that are in a ready-to-use format. Now, since then, of course, all of the other glass manufacturers, for the most part, have now washed and sterilized glass also. First-in is very important with these things and Stevanato also has good technical capability, and so, they've been able to really make a place for themselves in that segment of the market.

Shane Sullivan: How are you thinking about Gerresheimer? They've also talked about the move toward ready-to-fill or ready-to-use formats, as you just described. Do they face an uphill battle?

Fran DeGrazio: Sure, anybody that's coming in in a secondary position faces an uphill battle. BD is the leader when it comes to syringes. There are other players out there for sure that are good, but they'll always be the first name that people will think about and go to.

Part of it, again, you go back to the prior question when you asked, why do people choose. Well, one of the big things is around capacity and also the fact are you a proven entity. The pharmaceutical industry is very risk-averse, so they're going to go with a proven entity, too. Which is why one of the challenges is any time that

there's a new product or a new innovation, it takes an extended period of time to really pick up where you can start to see some real growth because you need to prove that you're able to deliver on it over an extended period of time.

Shane Sullivan: Moving on to the next category, what have you found to separate companies like West, Datwyler, and AptarGroup in the realm of elastomeric components? Considering West's commanding share in the elastomeric components category overall, is it logical to expect similar dominance in GLP-1s?

Fran DeGrazio: Well, that's going to be pharmaceutical company-specific, too. I'm sure that West is in the mix, but probably the other suppliers are somewhat in the mix, too, because of just the fact that there's a certain amount, the volume of what you're talking about, and the potential, the risk aversion that we're talking about. Certainly, they may all be in the mix. I can't tell you specifically, of course, who is and who isn't, but they are leaders in this space, and so, I would expect them to definitely be involved in the business.

Shane Sullivan: In more general terms, can Datwyler and AptarGroup match West's highest-value offerings like NovaPure? I've heard commentary that AptarGroup, for example, is several years behind from that technical standpoint. Do you tend to agree?

Fran DeGrazio: Yes, I think they come out with and they have come out with newer products, but usually what you've seen historically is West is leading with what they come out with and the other two will then follow up. As I mentioned, it's that first in that really gets you the lead in the marketplace. It's also, though, really understanding what customers need, and what they're looking for, and anticipating that. I think that's something that with NovaPure, in particular, was done well at West.

Shane Sullivan: We have a question from the audience, Fran, I will read it verbatim. "What is the reputation of Aspen Pharmacare as a manufacturer? Are they looking to be part of the GLP-1 manufacturing chain? What do you expect for Aspen?"

Fran DeGrazio: I'm not familiar with them, so I really can't comment.

Shane Sullivan: No worries. As we did with each of the relevant categories thus far, how would you characterize the current landscape for contract-manufactured drug delivery devices, let's call them, so essentially, who is making these pens and autoinjectors that are used for GLP-1s?

Fran DeGrazio: I think there's again a mix of how that's being done. Even within the pharmaceutical companies themselves, they may have different strategies as to what they outsource and how much they outsource versus what they may do even internally, to a certain extent. I know the designs of the delivery system itself is owned by the customer, by the pharma company, so that means that they can go and have that produced at a contract manufacturing organization or multiple contract manufacturing organizations. I think because of some of the challenges in producing such large quantities, they're always looking at doing that within several different suppliers.

Shane Sullivan: Yes, it seems like capacity is critical. Just to make sure, who is active in that space? I know West

has a contract manufacturing business for those types of products. Anyone else that you'd highlight?

Fran DeGrazio: Not off the top of my head. There are, of course, several others, but they have all gone through name changes and such, and so, I don't really have them off the top of my head.

Shane Sullivan: Fair enough. With regards to that IP piece, of course, Novo and Lilly, they own it, as you just alluded to. Are there any proprietary higher-margin systems players that could capture some portion of the GLP market, meaning they have their own kind of pen technology? Or do you envision that paradigm staying as is?

Fran DeGrazio: The question being, do you think someone could come in with a better delivery system? Is that what the question is?

Shane Sullivan: Exactly, you got it.

Fran DeGrazio: There are other delivery systems out there, but I am not aware that any of them are going to necessarily be better than what's already out there currently. Certainly, there are other organizations and even smaller startups trying to come up with different ways of just different GLP-1s, for instance, that would be competitive to the products currently in the marketplace. There's also a lot of activity in the oral space. At this point in time, well, the Rybelsus is a GLP-1 that's oral, but it seems to not have made a significant dent in the injectable space. I don't anticipate that there's a real significant driver for a totally new injectable delivery system for this space.

Shane Sullivan: I know you mentioned pre-call that you can't break down the cost components, so we can skip that topic. One theme so far has been capacity and I just want to get a sense of where the industry is in that respect. Do you think that the recent demand for GLP-1s for obesity has come as a surprise to the suppliers in this space? How would you characterize the current bottlenecks and how serious they are? When could such constraints normalize?

Fran DeGrazio: Well, I would say it's probably somewhat of a surprise. This is just a guess based on, really, the communication is typically there between the customer and their supplier but, quite often, until there's actually clarity around what that forecast is going to be, then, of course, it takes a period of time to build to be able to reach that demand. That, I think, is the challenge, that there is an extended period of time to bring in new tooling, and get things validated, and such. All of that will be addressed over time, but it just does take a period of time to get that done. I think that all suppliers are trying to address those kinds of issues, especially after the challenges of COVID.

Shane Sullivan: Are there specific categories - I've heard glass shortages mentioned frequently - that you would highlight?

Fran DeGrazio: Yes, I think that's probably one of the biggest would be the glass shortages. I think almost every glass supplier has put in additional capacity or is putting in additional capacity. You're talking about significant capital investment and, in some cases, actually new buildings that are going in, it's not only

equipment, and so, that does take an extended period of time. You see what now, which I think is a good move on Stevanato's part, to go into the U.S. into Indiana, and certainly that will be to produce a lot of glass, and I'm sure some of it will be supporting Lilly in some way would be my guess.

Shane Sullivan: Considering the challenges that come with sourcing, could you describe how pharmaceutical companies weigh primary, secondary, and tertiary supplier mix from a risk mitigation standpoint? There seems to be a trade-off, if you will, between volume with a certain manufacturer, maybe that results in better pricing, versus hedging against shortages, as seems to have been the case with glass.

Fran DeGrazio: Years ago, this philosophy, and if you go back to Deming in the '80s, the quality philosophy was to single source, and single sourcing was recommended because that way you could work with one supplier and you both win-win. If they had issues, you work together, and you make the improvements, and everything's good going forward.

However, the philosophy now has changed through the years, and so, even the FDA through the COVID situation, recommended evaluating secondary sources of supply. In many cases, you're taking someone that might have been selling at 100% of their volume to you and saying, "Ok, I'm going to evaluate or I'm going to qualify a second source." Then there comes a decision to be made: is it going to be an active second source or is it just someone that you have approved and on the shelf for potential in the future?

If they're really going to be active, which is the only way that you can know and stay on top of have they made any changes or anything like that, then they've got to be active in some way. Typically, that would mean an 80:20 split. If you were getting 100% of your glass from supplier X, now, you would go to 80% at supplier X and 20% at supplier Y. That would be, at least initially, how something like that would start out. It doesn't mean eventually it couldn't go to 50:50, but I would think that they'd have to earn that over time, proving that they can deliver on what's necessary.

Shane Sullivan: Is that all spec'd in ahead of time to the drug's master file, the secondary supplier?

Fran DeGrazio: It may or it may not be. It all depends on how the regulatory group files. In some cases, they may file in very general terms, and so, they can get away with making an adjustment like that without having to redo a filing. In other cases, they may be very specific, even down to a manufacturing site, and so, that then is much more involved. It all depends on the conservative nature of the regulatory team.

Shane Sullivan: I know we're pressed for time, so I'll work in one last question. I think there are three considerations we haven't touched on yet just in terms of the evolution of the GLP-1 category. Oral GLP-1s, pipeline GLP-1s like retatrutide which might require different packaging components, and eventual rise of generics. If you could weigh in on those three aspects, I think that'd be a good place to wrap up.

Fran DeGrazio: I think there certainly is activity in the oral space. For instance, I know Pfizer had an oral that they were looking at going to, by the end of the year, make decisions about their Phase 3 late-stage trials. I just read something, though, recently that said they have put a halt to that because they found that liver enzymes were out of whack. I don't know if that's the exact same product, but there's definitely activity in the oral space.

That may be something down the road that could have an impact, but it won't be for at least several years.

As far as other GLPs, I think it's only a matter of time. They'll continue to develop alternatives and better alternatives, and so, I can imagine that that will happen, especially with a focus on the obesity market. I forget what the third category was.

Shane Sullivan: Generics - will they have the same packaging requirements as their branded predecessors?

Fran DeGrazio: Yes, typically generics and biosimilars will understand what the originator used and then will try to use something very similar. That's at least typically what has happened. They still are going to have to prove it works with their specific generic version of the drug product. There can always be some differences in some of the excipients and things of that nature at times with generics.

I do think, though, when you talk about a delivery system, if you go generic and you say, "Ok, now, instead of using this prefilled syringe system in an autoinjector, because it's generic and I want it to be lower cost, I'm going to drop the autoinjector." They're not going to win because now you're talking about patients that are self-administrating, and so, the system that they use to deliver has got to be at least comparable from that standpoint. You can't make it harder for the patients.

Shane Sullivan: Fran, we've run out of time, so we'll have to wrap things up here. Thanks so much again for participating. It's been a helpful discussion. For those in the audience listening in, if you're interested in scheduling a follow-up call, please get in touch with your Guidepoint representative. Otherwise, I hope everyone has a good rest of their week. Fran, thanks so much again. It's been a pleasure.

Fran DeGrazio: Take care. Bye-bye.