Roundtable Session 1 – Table 15 - Wide-Spread Adoption of High-Volume Delivery Subcutaneously: What's the Hold-Up?

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Abstract:

As advancements in biologics and patient-centric solutions drive the need for high-volume subcutaneous (SC) drug delivery systems, their adoption in clinical practice remains slower than anticipated. This roundtable discussion will delve into the multifaceted challenges of SC delivery for large-volume therapeutics across drug development, device innovation, and regulatory landscapes. Key areas of focus include:

- Technical limitations / design challenges of current delivery device technology.
- Evolving regulatory requirements for combination products.
- Patient perspectives, considering comfort (pain/tolerability), usability, adherence, and overall satisfaction with SC delivery systems.
- Integration of high-volume SC delivery into clinical workflows and healthcare systems.

Join us for an engaging discussion as we explore strategies to reshape the treatment landscape and enhance quality of care for patients.

Discussion Questions:

1. What are the primary technical challenges in designing devices for high-volume subcutaneous delivery, and how can innovations in drug formulation and device technology address these issues?
2. How do regulatory frameworks and agency expectations impact the adoption of high-volume SC delivery systems, and what strategies can be employed to navigate these challenges?
3. From a patient perspective, what factors (e.g., comfort, usability, injection time) most influence the acceptance of high-volume SC delivery, and how can these be better addressed in product design?
4. What role do healthcare providers and payers play in the adoption of high-volume SC delivery, and how can manufacturers effectively engage these stakeholders to drive acceptance?
5. How can cross-functional collaboration between drug developers, device manufacturers, and regulators accelerate the commercialization of high-volume SC therapies?

Notes:

Define high volume:

- 5 mL without enhancers
- Up to 25 mL with enhancers (eg hyaluronidase)

Consider route of administration:

- Mainly focused on subcutaneous (SC) delivery; intramuscular
- Many IV products develop SC line extension due to competitive landscape (oncology products)
- Improve patient experience/convenience by decreasing delivery time, enabling home use, or administration at outpatient center

Consider delivery time:

- Delivery time of ≤ 30s (target of 5-10 second) for pre-filled syringes (PFS), autoinjectors, on-body-injectors (OBI)
- Storage time of >24 hours for some OBI (drug product stored in device) and then delivery

Hyaluronidase and permeation enhancers

- Exclusivity deals between Halozyme and companies for targets can hinder development
- Halozyme US patent for rHuPH20 expiring in 2027 which may open the market for other hyaluronidase developers or for companies to develop hyaluronidase internally to support high-volume SC delivery
    - Follow up: New European patent issued for Halozyme ENHANZE rHuPH20 drug delivery platform in 2024 (expires 2029)

Considerations that can impact injection site pain

- Increased volume and shorter injection time
- Formulation viscosity, salt content
- Impact of pH can be difficult to predict (eg same degree of pain for drug product at pH 4.5 and pH 7.0)

Does industry understand the goal post for developing large volume subcutaneous products? What is the perspective of clinicians and patients?

- Shorter injection times?
    - Aim for 10-30 seconds but this is more of a company goal than a patient requirement
- What is the perspective on injection site pain?
- Infusion center vs outpatient clinic vs home use?
- What is the perspective on number of injections and injection site (abdomen, thigh, arm)?

Development of devices for large volume delivery

- Glass (heavy) vs plastic syringes (consider patient use and cost)

    - Particulate testing for PFS – concerns around compatibility with silicone oil, surfactants
    - Can characterize particles and develop control strategy around silicone oil particles (complicated)
    - Silicone oil particles could be a concern for ophthamology products
    - Silicone free PFS available
- Not a lot of on-body injection devices on the market – 5 mL autoinjector more common
- Many companies provide vial to use with off-the-shelf injection pump available at HCPs
    - Freedom Infusion Systems used with for at home immunoglobulin treatment (Primary Immunodeficiency Diseases (PIDD)); CADD-Legacy Intravenous pump
- What are the regulatory expectations (eg cross labeling)
    - Blincyto labeling strategy is infusion pump agnostic
        - Different infusion durations (24 hrs to 1 week)
    - Disposable product contacting components
        - consider compatibility; perform hazard risk assessment to enable use of any device
- If you're partnering with a company, how much control/influence do you have in device development?
    - May not want to develop product specific devices
    - Application for different SKUs can be challenging
    - One set of materials
- Neulasta Onpro on-body-injector designed to deliver dose on day after chemotherapy (outpatient) – dose must be stable and compatible with components while worn by patient
    - Conditioning; shipping validation / simulation
- Need to really understand how device will be used
        - e.g. wear for 24 hours (stability and agitation (simulate walking, etc)
        - e.g. deliver 20 mL over 2 hrs or single use deliver over 30 min
        - single use device or reusable device with disposable parts?

<u>Immunogenicity concerns</u>

- Increased immune response for subcutaneous injections than intramuscular
    - SC delivery traffics to lymph nodes more effectively
- Products may have different labels in different markets (ie SC in one market and IM in another)
    - Different clinical assessments and bioavailability
    - Different volume limits (ie > 5mL IM vs 2-3 mL SC)

<u>Payer reimbursement</u>

- Understand basis for payer base and process for price negotiations in EU
    - Focus of price negotiation is on efficacy and not convenience – payers want evidence of improved compliance with device
    - Life cycle management and impact of introducing new device on price negotiations

        - Companies perform cost/benefit business assessment for launching with device vs introducing device post launch and starting new price negotiations
- FDA draft guidance on Patient Preference Information (PPI) in Medical Device Decision Making
    - How is collecting patient feedback build into clinical protocol

What could accelerate development of large volume products?

- Educate cross-functional partners and regulators?
    - Device demos
- Patient driven cases
    - Availability of GLP-1 agonists may shift patient comfort with self-administered subcutaneous injections
    - Familiarization with technology may lead to more engaged patient advocacy
- Payers dataset/database
    - Patient preference models based on interviews
    - Information internal but not globally available
- Seat at the table with clinical/commercial development groups
    - Understand commercial patient preference early so that it is included in clinical strategy (e.g. at dose escalation, FIH)
- Patient centric drug development means drug delivery is central
    - Drug delivery considerations/route of administration is built into all phases of development