AAVBC

American Academy
of Value Based Care

AAVBC Medicare Part B IV/IM (Physician administered) to Part D SubQ (Patient self-administered) Utilization

Quick Reference Guide

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AAVBV Medicare Part B IV/IM (Physician administered) to Part D SubQ (Patient self-administered) Guide

1. INTRODUCTION: IV/IM and SubQ ADMINISTRATION PRIMER

Value-Based Care (VBC) models encourage shifts in drug delivery that improve patient outcomes and reduce costs. One emerging strategy is transitioning eligible injectable medications from **Medicare Part B** (typically IV/IM infusions in clinics) to **Part D** (self-administered subcutaneous injections at home). This initiative hinges on recent advances that make self-injection feasible without sacrificing efficacy, while navigating Medicare's coverage rules. By empowering patients to self-administer when appropriate, providers can enhance convenience and potentially lower total medical spending. Below, we outline the clinical rationale, regulatory landscape, and operational tactics for a successful Part B-to-D drug transition program in a VBC framework.

Formulations and Bioequivalence:[1-3]

High-concentration biologics face formulation challenges (viscosity, aggregation) that historically required IV administration, but new solutions are enabling subcutaneous (SubQ) versions. Manufacturers are using **viscosity-lowering excipients** and advanced device designs (autoinjectors, wearable pumps) to allow large doses in small volumes.

- **Overcoming Dose Volume Limits:** Historically, SubQ delivery was limited to small volumes (typically 1–2 mL), posing a challenge for high-dose biologic drugs. Newer technologies now enable the delivery of larger fluid volumes (often >3 mL).[1]
- **Managing Viscosity and Concentration:** High drug concentration, often required for high doses, can increase **viscosity** and lead to formulation instability (e.g., aggregation). Manufacturers utilize excipients (like salts and amino acids) and specialized formulation technologies to reduce viscosity.[1]
- **Role of Hyaluronidase:** Many SubQ formulations are **co-formulated with recombinant human hyaluronidase (rHuPH20)**. Temporarily breaks down the hyaluronic acid barrier in subcutaneous tissue, allowing for the rapid dispersion and absorption of large-volume injections.[1]

Equivalence and Dosing:

- **Pharmacokinetic (PK) bridging studies** are the standard regulatory approach to confirm that the SubQ dose achieves drug exposure comparable to the approved IV form (non-inferiority)[1-4]
- Goal is for fixed-dose SubQ regimens to match the efficacy of weight-based IV dosing[1, 5]
- **Clinical Vigilance is Required:** Clinicians must be mindful that **flat SubQ dosing** (not based on weight) may risk under-dosing in patients at the extremes of body weight, necessitating monitoring and potential dose adjustment[5]

Immunogenicity and Long-Term Safety:

The **route of administration** can affect how the immune system recognizes a drug, influencing long-term efficacy. However, in clinical practice, the **incidence of anti-drug antibodies (ADAs)** is generally **similar between subcutaneous (SubQ) and intravenous (IV) routes** for most biologics, and the theoretical increased immunogenicity with SubQ delivery **rarely leads to clinically significant differences** in safety or effectiveness.

- **Risk of Anti-Drug Antibodies (ADAs):** The subcutaneous space contains specialized antigen-presenting cells (APCs)
  - Since SubQ administration brings the drug directly into contact with these cells, there is a theoretical potential for an **enhanced immune response**, leading to the development of **Anti-Drug Antibodies (ADAs)**.[1, 6]
  - **Impact on Efficacy:** An ADA response can potentially **impact the drug's pharmacokinetics and efficacy**, which is a significant clinical risk for long-term chronic therapy.[1,6]
- **Current Evidence:** While some individual therapeutic proteins have shown a higher incidence of ADAs with SubQ administration, a recent meta-analysis comparing 17 therapeutic proteins found **no statistically significant difference in ADA incidence between the IV and SubQ routes overall.** The specific therapeutic protein itself, rather than the route, appears to be the most significant factor.[1]

Quality of Life (QoL) and Patient Preference[7]

- A 2024 meta-analysis of 30 studies found that **83% of adults with immune-mediated disorders** preferred **subcutaneous (SubQ)** administration over **intravenous (IV)** therapy, citing greater **convenience, flexibility, and autonomy.**
- Patients reported **lower emotional distress** and **higher treatment satisfaction** with self-administered SubQ formulations, primarily due to reduced clinic time and greater control over scheduling.
- Transitioning to home-based SubQ delivery has been associated with **improved adherence** and **reduced treatment fatigue** compared with traditional infusion-center models.

Clinical efficacy and safety[7,8]

- SubQ administration achieves **comparable efficacy and pharmacokinetics** to IV formulations across multiple biologic and immunoglobulin therapies
- **SubQ immunoglobulin (SubQIG)** produces **more stable serum IgG levels**, fewer systemic adverse effects (e.g., headaches, chills, fatigue), and **lower incidence of infusion reactions** than IVIG
- SubQ therapy allows for **smaller, more frequent doses**, improving physiologic tolerance and patient independence without compromising clinical outcomes