Guidance for addressing payor limits on dose increases (e.g., infliximab 5 mg/kg to 10 mg/kg) or limits on dosing frequency (e.g., every 8 weeks to every 4 weeks)

Many pharmaceuticals have dosing parameters that support a maximum dosage per body weight or body surface area or a set maximal dosage independent of patient body size.[1] These maximum doses are product specific, and, in some cases, disease state-specific and are defined in the U.S. Food and Drug Administration (FDA)-approved product prescribing information and/or in national compendia and other peer reviewed resources. The goal of dosing or frequency limitations is to ensure appropriate utilization of medications based on FDA-approved dosing, nationally recognized compendia, clinical practice guidelines, and peer-reviewed medical literature while promoting safe, effective, and cost-effective use of prescription drugs. In addition, these limits may prevent stockpiling, diversion of medications, or cost.

Requests for quantity limit exceptions will be considered based on factors such as the diagnosis, prescribed dosage regimen, previous treatment history, and the prescriber's clinical rationale for exceeding the established limit.[2] Plans will often consider evidence from FDA-approved labeling, nationally recognized compendia, clinical practice guidelines, and peer-reviewed literature to support an exception to a dosing limit.

QUICK REFERENCE

Key documentation for dose or frequency exception requests

Clinical justification

Document the specific reason for exceeding dosing limits:

- Fistulizing Crohn's disease
- Persistent symptoms or inflammation despite standard dosing
- Subtherapeutic drug levels or loss of response
- Hypoalbuminemia or high inflammatory burden

Include phrasing such as:

- "Ongoing disease activity despite standard dosing"
- "Partial clinical response at 5 mg/kg"

Treatment history

- Prior medication use and response
- Dosing timeline (initiation, titration, escalation)
- Previous dose at which therapeutic failure occurred

Objective measures of disease activity

- Fecal calprotectin
- C-reactive protein (CRP)
- Endoscopic findings
- Therapeutic drug monitoring results (if available)
- Physician global assessment

Safety and tolerability

- Confirmation of no adverse events or toxicity at proposed dose
- Ongoing monitoring plan in place

Coding and documentation

- ICD-10 code to most specific level (e.g., K50.13 vs. K50.9)
- Most recent progress note documenting disease status
- Relevant labs or imaging findings

Supporting guidelines and evidence

- FDA-approved product labeling
- Nationally recognized compendia
- Clinical practice guidelines
- Peer-reviewed studies (especially for off-label or non-standard dosing)

Clinician -led	Staff -led	Key step	Key considerations
	✓	Evaluate maximum dosing requirements	☐ Check if the prescribed dose exceeds established maximum dosing per body weight, body surface area, or set limits based on the drug's FDA-approved prescribing information, compendia, or clinical guidelines ☐ Product-specific max dose verified ☐ Disease-specific considerations reviewed
✓		Confirm clinical circumstances supporting the exception	☐ Document the patient's unique clinical situation that necessitates a higher dose beyond the plan's limit. Examples: ○ Variations in weight or body surface area ○ Variability in drug metabolism or pharmacokinetics requiring dose adjustments (e.g., subtherapeutic drug levels, high inflammatory burden, or hypoalbuminemia) ○ Increased disease severity (e.g., fistulizing Crohn's disease or persistent endoscopic disease activity despite therapy) ○ Include drug levels where appropriate, increasingly being requested by payors during reauthorization or continued high-dose requests ○ Other: _____
✓		Provide clinical rationale for exceeding the limit	☐ Check applicable factors and provide supporting documentation: ○ Changes in the patient's weight, metabolism, or disease progression that justify a higher dose ○ Continued need for the current dose to maintain efficacy or prevent disease progression ○ Inadequate response or loss of efficacy at the plan's limit ○ Other: _____ ☐ Consider including phrasing like: ○ Partial clinical response ○ Persistent symptoms ○ Ongoing disease activity despite standard dosing ○ Changing to an alternative medication prior to a trial of dose escalation may risk developing anti-drug antibodies and limit future use of this medication
	✓	Provide supporting documentation	☐ ICD-10 codes to the highest specificity (e.g., Crohn's of small intestine with fistula, instead of non-specific Crohn's disease) ☐ Treatment history and prior response to lower doses ☐ Objective measures (e.g., lab results, imaging reports, functional assessments) ☐ Notes from patient visits documenting disease status ☐ Consistently document objective measures of disease activity: ○ Fecal calprotectin ○ CRP ○ Endoscopic findings ○ Physician global assessments

Clinician -led	Staff -led	Key step	Key considerations
✓		Assess safety and tolerance	☐ Confirm that the patient has not experienced any adverse effects or drug toxicity at the requested dose: ○ No treatment-limiting side effects ○ No signs of drug toxicity ○ Ongoing monitoring plan in place
✓	✓	Cite relevant guidelines and evidence	☐ Review evidence supporting the exception: ○ FDA-approved product labeling ○ Nationally recognized compendia (e.g., American Hospital Formulary Service [AHFS] Drug Information, Micromedex drug database, and UpToDate Lexidrug) ○ Clinical practice guidelines ○ Peer-reviewed medical literature
	✓	Submit the exception request	☐ Completed exception request form ☐ Supporting clinical documentation
✓		Prepare for potential follow-up	☐ If the request is denied: ○ Review the denial letter to understand the reason ○ Consider appealing the decision, including new evidence or documentation (CCF.org has appeal letter templates for medication dose escalation requests) ○ Prepare for a peer-to-peer discussion (timing may vary based on different state regulations)

References

1. FDA Dosage and Administration Section of Labeling for Human Prescription Drug and Biological Products — Content and Format Guidance for Industry. Published January 2023. Accessed February 3, 2025. https://www.fda.gov/media/72142/download

2. Exceptions. CMS.gov. Accessed February 3, 2025. https://www.cms.gov/medicare/appeals-grievances/prescription-drug/exceptions