Pharm-Olam
Helping Create A Healthier World

Predictive Resupply

An Analytical Method of Managing Drug Inventory in Clinical Trials

Introduction

In the floor-and-ceiling drug resupply method, an inventory management system restocks drugs up to a site's storage capacity, or "ceiling" level, whenever it has been depleted to protocol minimums (the "floor" level). Typically, individual unblinded drug types (e.g., active and placebo) are counted separately for the floor level, and whenever either type reaches floor level, both types are restocked to ceiling level.

The floor-and-ceiling method is not adequate for all studies. In fact, floor-and-ceiling resupply may adversely affect a site's ability to comply with study protocol. The method can result in too many shipments, costly drug oversupply at sites, or even insufficient on-hand supply. That's because in some studies, the protocol is structured such that drug dispensation varies widely over time.

Suppose a drug is dispensed at a rate of one bottle per week for the first four weeks of the trial, and in the fifth week the entire next month's supply is dispensed all at once. Suppose, too, that patients are enrolled and prescribed the treatment plan on a rolling basis. In this example, even though the rate of drug dispensation is usually one bottle per week, the floor level must be kept high enough to accommodate each patient's fifth week visit, because not all patients will have entered the study at the same time. If floor inventory level is set too low, the site risks not having enough drug on-hand to dispense to patients, potentially jeopardizing valid data, or even the entire study.

Furthermore, suppose our example applies to a therapeutic area or indication with a high dropout rate. Keeping sufficient inventory for each patient's fifth week might prove excessive if many patients exit the trial before their fifth week. Sponsors may also cite shipping costs, or costs of the drug itself, as additional reasons to avoid oversupply.

Rationale for Fixing the Floor-and-Ceiling Problem

For study protocols designed to have multiple dispensing visits, Pharm-Olam recognized an opportunity to optimize its inventory control process. By analyzing orders and other data captured by its inventory management system, it could anticipate sites' demand for a drug, greatly reducing occurrences of oversupply or insufficient drug inventory. The anticipatory approach to managing inventory, which it has called Predictive Resupply, would therefore save significant time, energy and resources.

Solution

Logistically, an optimized drug distribution supply chain has two key dependencies: a study team, who must define an efficient resupply algorithm, and an inventory management system, which must be capable of operating based on the team's algorithm. Pharm-Olam's Predictive Resupply algorithm makes use of the five key data points:

1. Dispensation Volume: How much drug is dispensed at each visit?

A schedule is created that lists each dispensing visit, and the amount of drug that will be dispensed to patients at each visit. If a variable amount of drug is allowed, the maximum amount possible should be listed. It may be possible that different randomization treatments dispense different amount of drugs. In that case, these treatments should be accounted for separately.

2. Safety Stock: How much drug should be reserved at each site?

"Safety Stock" is the amount of drug that must be reserved at a site after all dispensing calculations have been performed. Where applicable, it is intended to support newly randomized patients, who by definition cannot be predicted. It also supports replacement assignments in the event of missing, broken, or unexpectedly quarantined drug containers.

3. Timing: How far into the future does the algorithm expect sites will need supplies?

Timing is a significant factor in determining whether Safety Stock will be depleted. To preempt the possibility of depletion, the Predictive Resupply algorithm will use two date-driven variables: the "look ahead" threshold, measured in days or weeks, and the "resupply" threshold, also measured in days or weeks.

Suppose the "look ahead" threshold is two weeks and the "resupply" threshold is eight weeks. If, based on upcoming visits in the next two weeks, the site is not expected to have enough drug on-hand to maintain its Safety Stock, Predictive Resupply will trigger a shipment to the site such that at the end of eight weeks of visits, the site will still have a full Safety Stock.

4. Patient Eligibility: What determines whether a patient is eligible for resupply?

Predictive Resupply will only count patients who are actively taking drugs. Subjects who are not randomized will not be eligible. Similarly, patients who discontinue using the study drug will be deemed ineligible for resupply.

These resupply eligibility criteria are not intended to be exhaustive. Other special requirements for eligibility, based on the study's design, should be considered and fully defined in order to ensure the most effective use of the algorithm.

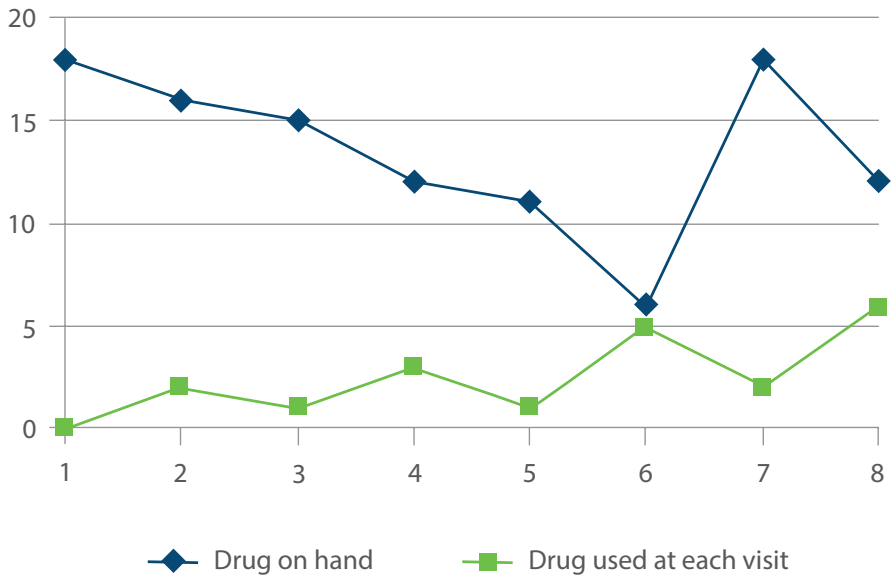
5. Frequency: How often should the Predictive Resupply algorithm run?

Ideally, the inventory management system would run the algorithm at regular intervals (e.g., once every night). However, the algorithm can run less often if prudent or if desired by the study administrators. To ensure effective performance of the algorithm and that sites always have sufficient drug inventory, it is not advisable to run Predictive Resupply any less than twice per "look ahead" period.

Examples of the Benefits of Predictive Resupply

In this section, we will demonstrate visually the differences between the floor-and-ceiling and Predictive Resupply methods.

Inventory Levels Using Traditional "Floor and Ceiling" Resupply



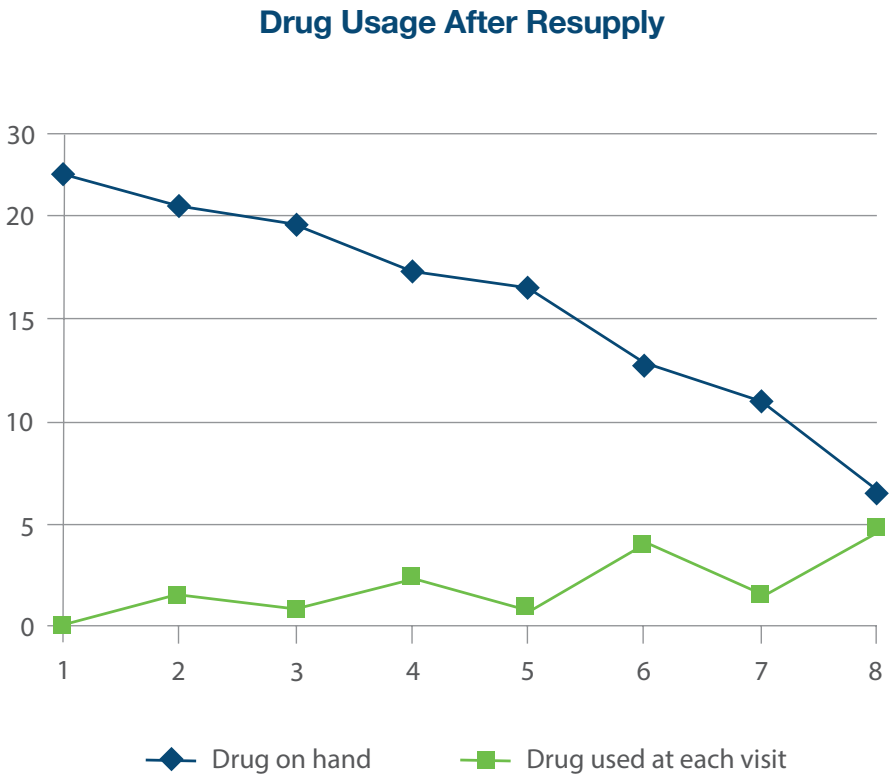
In the above example, the floor is set at eight units, and the ceiling is set to 18 units. The site begins with 18 units of drug on hand (the "Ceiling").

Note the variability in dosing, particularly in the later visits. At week six, the amount of inventory needed by one patient is perilously close to the amount on hand (five units needed, only six present at the site.)

The floor-and-ceiling system will trigger a new shipment before the patient's visit during week seven. However, if the site had two or more concurrently enrolled patients, it would be at high-risk for inadequate inventory. In traditional models, either the floor or the ceiling must be raised to allow for variability, but either would require potentially unnecessary inventory idling at a site.

In the following example, predictive resupply is employed, utilizing the following parameters:

- **Safety Stock:** 8 units
- **"Look ahead":** 2 weeks
- **"Resupply":** 8 weeks



Now, the site will have exactly 8 units of drug (their Safety Stock threshold) on-hand at the end of the resupply window.

Calculating the Amount to Ship

The amount of drug to ship to a site uses the following formula:

$n = P + S - H$

n = Amount to ship
P = Total amount predicted in the resupply window
S = Safety Stock
H = Drug inventory already on-hand at the site

The total amount predicted in the resupply window is a summation of all individual subject dispensing needs over that time period. Subjects who are not randomized or who have ended treatment will not be counted towards this summation.

It should be noted that, while the initial inventory is larger than the floor in the previous example, the administrators have a more robust level of control. In short, the project can modify the safety stock, look-ahead weeks, or resupply weeks to optimize the amount of drug on-site without necessarily raising the total amount needed.

About Pharm-Olam International

Pharm-Olam International is a global contract research company with a presence in over 40 countries, offering a wide range of comprehensive clinical research services to the pharmaceutical, biotechnology, and medical device industries.

For more information on Predictive Resupply, contact **info@pharm-olam.com**.

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