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% of Medication taken: Accounting  
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patient forecast

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*Patient compliance is a common feature of patient-based drug forecasts, although the incorporation of drop-out is an aspect that is often neglected. Although 'standard' therapy compliance rates may be summarily applied, accounting for both compliance and drop-out is often perceived as daunting. Pangolin PharmaTech has developed a model to calculate the actual percentage of medication taken for a specific patient forecast using the compliance and drop-out rates. The calculation behind the scenes is rather complicated and could appear as a 'black box'. However, this simple user guide deconstructs the calculations, describing the thinking behind each step in a linear manner, and demonstrating one approach for incorporating both elements into your forecast.*

## **Compliance and the percentage of medication taken**

Medication compliance (adherence) refers to the degree that a patient conforms with the aspects of timing, frequency and dose of a prescribed therapy regimen. Most pharmaceutical volume forecasts simply include a single annual compliance rate when converting patients to volume, making it easy to overestimate the true percentage of medication taken. Even if a reliable estimate of the compliance rate is available, it is highly probable that the calculated volume measure (treatment days or units), and therefore revenue conversion, will be overestimated. This is because the compliance rate does not account for the fact that some of the patients in any given year will be new patients, and that not all of these patients will start their course of medicine at the beginning of the calendar year. Thus Pangolin recommends addressing the calculation using the concept of 'percentage of medication taken' to account for compliance within a patient population (with or without the additional consideration of drop-out).

## **Compliance and the new patient segment**

Consider the following situation: You are calculating the days of therapy from a patient forecast of a chronic (non-seasonal) product. The product should be dosed daily for 365 days per year, and your sources (e.g. market or desk research) indicate a compliance rate of 80%. Thus the patient who starts therapy in January can be expected to take 80% of their medication, while the patient starting in December will only take 1/12 of the compliant days of therapy.

Therefore, the new patient segment, in any given year (assuming that the distribution of commencement of therapy is equally spread over the entire year) takes only half of the annual treatment. In the case of a compliance rate of 80%, the percentage of medication taken will be 40%.

In the launch year (which consists entirely of the new patient segment), the percentage of medication taken should be further adjusted to account for the month of launch. For instance, if the drug is launched in April, the new patient segment receives only 38% of the yearly treatment (50% of

365 days \* 9/12 months). In the case of a compliance rate of 80%, the percentage of medication taken will be 30% (50% \* 80% \* (9/12)).

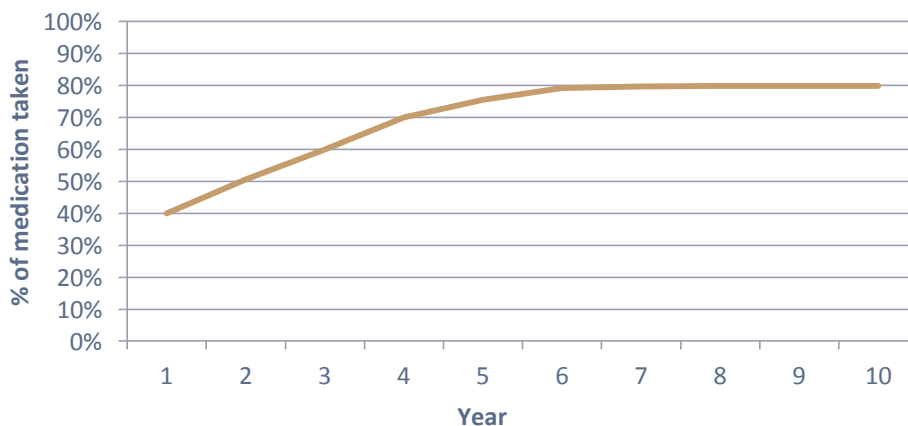
When considering subsequent years from launch year, the percentage of medication taken depends on two components: the compliance rate in the carry-over patients, and the proportion of new patients that join the treated patient pool over the course of the year. As time progresses, the proportion of on-going patients increases relative to the new patient segment, and so the percentage of medication taken approaches the target annual compliance rate of 80%.

Let's consider the following annual forecast of patient numbers for a chronic therapy, assuming that all patients continue on therapy from one year to the next.

**Table 1: Annual percentage of medication taken for a 10-year patient forecast, assuming 100% persistence**

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10
Number of patients in the forecast	800	3,000	6,000	8,000	9,000	9,200	9,300	9,350	9,375	9,400
Number of patients receiving only 50% of their treatment (new patients)	800	2,200	3,000	2,000	1,000	200	100	50	25	25
Number of patients receiving 100% of their treatment (carry-over patients)	0	800	3,000	6,000	8,000	9,000	9,200	9,300	9,350	9,375
% of medication taken	40.0%	50.7%	60.0%	70.0%	75.6%	79.1%	79.6%	79.8%	79.9%	79.9%

**Figure 1: Annual percentage of medication taken for 10 forecast years for the patient forecast detailed in Table 1**



## Drop-out and the percentage of medication taken

The patient drop-out rate refers to the rate at which patients discontinue therapy altogether. For example, if 100 patients are on therapy in Year 1, but only 80 remain in Year 2, then we have a drop-out rate in Year 2 of 20%. And similarly if we have 72 patients remaining in year 3, then the drop-out

rate in year 3 is 10%  $((80-72)/80)$ ). In general, the drop-out rate decreases over time, as more patients drop-out of therapy early on (as they experience adverse effects or lack of efficacy) while those that have been on the medication for some time, tend to continue with the therapy.

## The first year of treatment

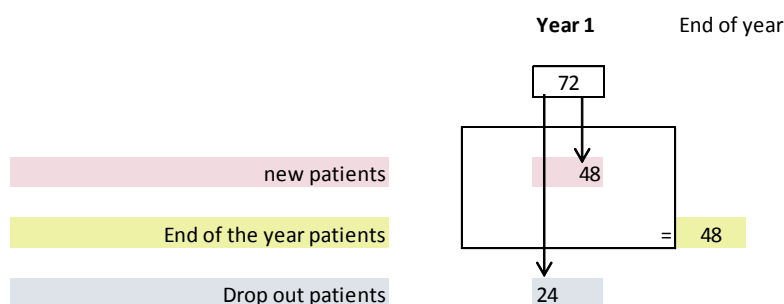
The calculation for the first year of treatment is simpler than for subsequent years, because despite the dynamics between patients initiating therapy and discontinuing therapy over the course of the year, only the number of patients actually on therapy at the end of year influences the number of days of therapy, and the percentage of medication taken. This is the number of patients generated for the launch year of the forecast.

Let us consider a simple case whereby we have 48 patients for our first forecast year. The same logic applies here as it did for the first year compliance explanation above, in that not all new patients will begin treatment at the start of the calendar year. Thus if we have 48 patients at the end of the year, and we maintain the assumption that all patients initiated therapy in an equal distribution across the year, this means that 4 patients receive treatment for the full 12 months, 4 patients receive treatment for 11 months, 4 patients receive treatment for 10 months, and so on.

The drop-out rate, perhaps counter-intuitively, plays no part in the calculation.

If the drop-out rate for the first year of treatment is 20%, this means that 60 patients started treatment, and 12 patients dropped out, allowing for the resultant number of patients on therapy each month of 4 (5 initiated minus 1 drop-out). Similarly, if the drop-out rate is 33.3%, this means that 72 patients started treatment and 24 dropped out, with the identical resultant number of patients on therapy each month of 4 (6 initiated minus 2 drop-outs).

**Figure 2: Drop-out patient dynamics in the first year**



## Subsequent years of treatment

In all subsequent years of treatment, the drop-out rate has an important influence on the number of days of therapy, and therefore, the amount of medication taken. Conversely to the compliance calculation, where the new patient segment is the most important consideration in the adjustment of compliance, when considering drop-out, it is the ongoing (or carry-over) patient segment that plays a key role.

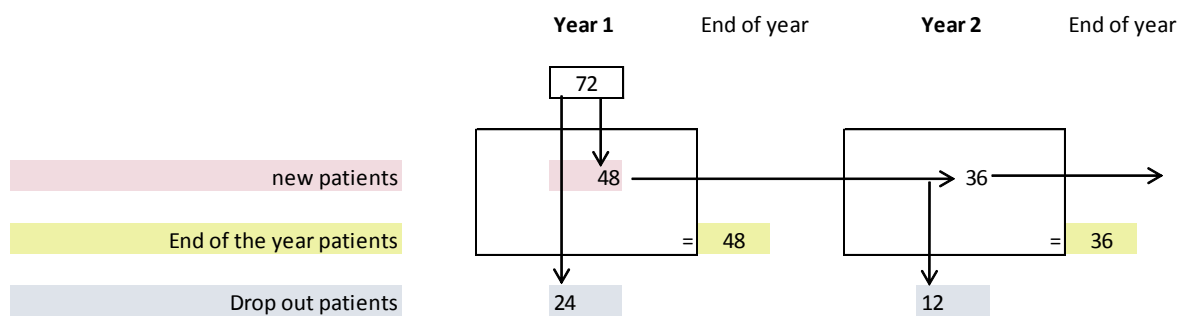
Let us consider a situation whereby patients are 100% compliant, but do not all persist with their treatment, such that the drop-out rate in year 2 is 25%. The result is that out of the 48 patients starting treatment in year 2 (carried over from year 1), 36 will still be on therapy at the end of year,

with 12 having dropped out. Not all patients will drop out in the first month, and those that drop out at the end of the year will, in effect, have taken a full 12 months of therapy. Similarly to the thinking behind the compliance calculation for new patients, by assuming the equal distribution of patients dropping out over the course of the year (i.e. one per month), the drop-out patients receive half of the therapy that a persistent carry-over patient will take. In this particular case, 36 patients receive full therapy and 12 receive half the duration of therapy. The resultant percentage of medication taken (adjusted for drop-out) is 87.5%.

$$(36 \text{ patients} * 100\%) + (12 \text{ patients} * 50\%) / 48 \text{ patients} = 87.5\%$$

This contrasts significantly to the theoretical rate of 100% that could easily have been summarily applied in a forecast setting.

**Figure 3: Drop-out patient dynamics in the first and subsequent years**



## Calculating the 'actual' percentage of medication taken

Doing an in depth calculation for the 'actual' percentage of medication taken that accounts for the combined aspects of compliance and drop-out, across both the new and continuing patient segments, rather than the simple application of a single compliance rate across all years, is a more robust way of generating the forecast volume for conversion into revenues.

Let us consider an example calculation for percentage of medication taken using a fictional patient forecast, with inputs for launch month, compliance and drop-out as detailed in Table 2.

**Table 2: Inputs for compliance and drop-out required to calculate the 'actual' percentage of medication taken for a patient forecast**

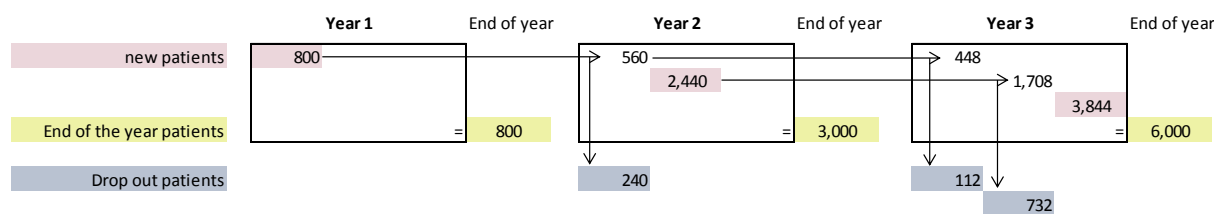
Input										
Forecast										
	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10
Patients	800	3,000	6,000	8,000	9,000	9,200	9,300	9,350	9,375	9,400
Month of launch	4									
Compliance and drop out										
Ongoing compliance	80%									
	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10
Patient yearly drop out % of treatment	N/A	30%	20%	15%	15%	15%	15%	15%	15%	15%

Apart from the year of launch of a new product, in every subsequent forecast year, the number of patients taking the product is a mixture of new, drop-out and carry-over patients.

The ‘actual’ percentage of medication taken needs to account for the change in dynamic between these new, on-going, and drop-out patients. Thus you are required to split your annual patient numbers into these different patient segments. Using the drop-out rate specific to your particular therapy area / product, you can apportion the patient numbers for each annual data point, using the on-going patients from the previous year, and the end of year number of patients (your forecast annual patient numbers) as a starting point.

Figure 4 shows a diagrammatic representation of the patient forecast that has been deconstructed into the different segments using the drop-out rate assumptions detailed in Table 2.

**Figure 4: Patient dynamics and longitudinal flow accounting for drop-out rate**



Only the carry over patients from one year to another receive a full year of treatment. As discussed earlier, the new patients and the patients who drop out take, on average, only half a year of treatment. In the year of launch, the new patients receive only half of the treatment, pro rata for the number of months the drug has been on the market.

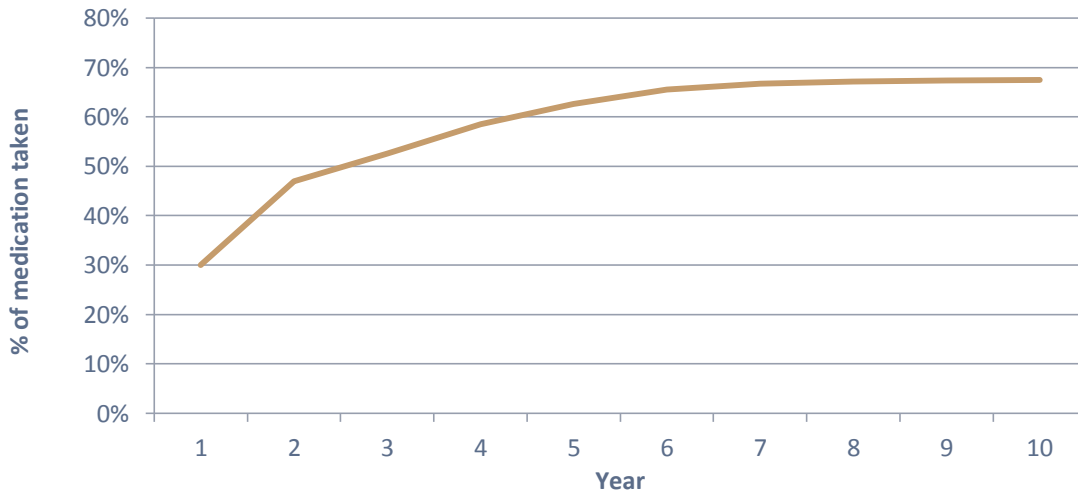
**Table 3: Calculated patient segments and their corresponding average annual percentage of medication taken**

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10
New patients in Year 1	800									
New patients in each subsequent year		2,440	3,844	3,562	2,869	2,105	1,896	1,803	1,764	1,759
Carry over patients that drop out		240	844	1,562	1,869	1,905	1,796	1,753	1,739	1,734
Carry over patients that remain on treatment		560	2,156	4,438	6,131	7,095	7,404	7,547	7,611	7,641
Compliance-adjusted patients	240	1,520	3,600	5,600	6,800	7,280	7,400	7,460	7,490	7,510
Theoretical total patients	800	3,240	6,844	9,562	10,869	11,105	11,096	11,103	11,114	11,134
% of medication taken	30%	47%	53%	59%	63%	66%	67%	67%	67%	67%

Detailed calculation Year 2:

$$(2440 * 50\% + 240 * 50\% + 560 * 100\%)*80\% / (2440 + 240 + 560) = 47\%$$

**Figure 5: The overall annual percentage of medication taken, accounting for compliance and drop-out rates**



**Demonstration: Comparing a forecast calculated using a single annual compliance rate with one calculated using the ‘actual’ percentage of medication taken**

Accounting for patient compliance, together with patient drop-out from therapy, and generating a precise annual input for the actual percentage of medication taken, allows for greater accuracy in the conversion of patients to treatment day, unit and/or revenue outputs.

The example below will take the reader through a comparison of a patient to treatment day conversion for a new product using a single annual 80% compliance rate versus the same conversion using the ‘actual’ percentage of medication taken calculated in Table 3 above. The treatment regimen for the product is recommended for 365 days per year.

**Table 4: Comparison of patient conversion to treatment days using percentage of medication taken vs a single annual rate of compliance**

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10
Number of patients	800	3,000	6,000	8,000	9,000	9,200	9,300	9,350	9,375	9,400
% of medication taken	30%	47%	53%	59%	63%	66%	67%	67%	67%	67%
Treatment days using ‘actual’ % of medication taken (000)	88	514	1,152	1,710	2,055	2,201	2,264	2,293	2,306	2,314
Treatment days using single annual compliance rate (000)	234	876	1,752	2,336	2,628	2,686	2,716	2,730	2,738	2,745

Over the course of ten years, the cumulated treatment days in this example are overestimated by around 27% when using a single annual compliance rate, which in figure 8, is graphically displayed as the difference in the area under the chart.

**Figure 6: Comparison of calculated treatment days using a single annual compliance rate vs the ‘actual’ percentage of medication taken**

