NEWDIGS
FoCUS Financing and Reimbursement of Cures in the US

FoCUS Individual Indication Workbook

The individual Indication Worksheet provides a step-by-step approach to financial management of a specific durable cell or gene therapy. The workbook contains four distinct worksheets:

Population Estimator

- Estimates incidence and prevalence by plan size and type.

Market Adjustment

- Adjusts population estimates to those that likely will be treated.

Therapy Impact Model

- Projects financial impact to your plan.

Solution Prioritization Tool

- Matches finance tools to organizational needs.

Once a specific disease is selected for analysis, the worksheets build upon each other to suggest potential financial tool(s) that may facilitate patient access and financial stability. A limited description of inputs and required data are provided on the worksheets. Additional detail and background are provided below for enhanced understanding.

Population Estimator

The population estimator tool allows the user to determine the incidence and prevalence of patients within the user's plan for a condition that may be treated by cell or gene therapy.

Step 1: Indication selection

Cell and gene therapies are categorized by therapeutic class, disease, and subpopulations. The options presented represent diseases and subpopulations with cell and gene therapy approved products or in clinical trials. Subpopulations are defined by the gene of interest in the clinical trial. If "ALL" is selected as the subpopulation, it will represent all individuals with the condition. It will not be limited to those with the gene of interest for which there is one or more products in development.

For purposes of the worksheet, incidence includes the onset of a disease as well as the "tipping point" of a condition for cell or gene therapy treatment. For example, the CAR-T therapies are currently used as a cancer treatment after other courses of treatment have been tried and failed. Incidence numbers for the CAR-T therapy would be projected based on numbers of individuals with the cancer for whom other treatments have not worked – they have reached a "tipping point" to treat with a CAR-T therapy.

Step 2: Payer type adjustment

The incidence and prevalence numbers provided in step 1 are based on the demographics of the total US population (General Population). The Population Estimator tool allows for further segmentation by Medicare, Medicaid or Not Medicare or Medicaid. Commercial plans, self-funded employer benefits, the Veterans Administration, Federal Employee Health Benefits, correctional health services, Tricare, the uninsured, Indian Health Services and all other categories of lives not included in Medicare or Medicaid are represented by "Not Medicare or Medicaid".

Incidence and prevalence differ by payer types as select diseases are more commonly associated with as age demographic characteristic of Medicare or Medicaid. For example, cancers are more frequently found in those over age 65 while genetic orphan diseases are often diagnosed at birth, an age demographic of Medicaid. These distributions are approximations however, as registries with age distribution by disease are not available outside of the SEER cancer registry. Selecting a payer type, however, does provide a better representation of incidence and prevalence estimates for the tool user.

Step 3: Population size adjustment

This section of the Population Estimator Tool allows you to take FoCUS's estimated clinically relevant incidence and prevalence estimates by payer type and apply simple population ratios to get the potential number of patients in your plan for individual product indications. The number of lives by category are presented in Table 1. Worksheet users should apply the number of lives by each line of business for best results.

Table 1 Lives by Payer Category for Population Model

Payer Category	Lives based on US 2020 census
Medicaid	70,225,000
Medicare	63,200,000
Not Medicaid or Medicare	198,075,000
US Population	331,500,000

Market Adjustment

The Market Adjustment Tool helps stakeholders assess the number of patients meeting FDA label treatment criteria that will likely be treated. Numerous factors beyond treatment eligibility will influence a product's use. The decisions to use a new cell or gene therapy, or market penetration, may depend on the disease severity, alternative treatments, insurance coverage, and/or other factors. The speed of adoption of, or ramp up to peak market penetration of the new cell or gene therapy is influenced by many of these same factors as well as market adoption factors similarly seen with chronic use treatments.

Step 1: Market penetration adjustment

Market Penetration is the number of individuals likely to be treated divided by treatment eligible individuals. In practice, the LIKELY TO BE TREATED population is expected to be smaller than the TREATABLE population.

For diseases with severe consequences, the likely treated/treatable percentage is anticipated to be high, subject to any challenges in identifying appropriate patients. For diseases with less severe or more long-term consequences, only a small percentage of eligible patients may be treated. Using an appropriate modifier is vital for any analysis, as the full eligible population may substantially overestimate the number of patients treated.

There is no simple way to anticipate an appropriate market penetration percentage, unfortunately, as market penetration is influenced by multiple factors that will vary in significance by disease. The Market Adjustment tool provides disease specific data for select factors that will influence market penetration.

> **Age at onset** – is the diagnosis in infancy, nearing the end of life, or in between?
> **Impact to life expectancy** – can an individual live with the disease or is life expectancy greatly shortened?
> **Therapeutic options** – are there alternative treatments? Are they sufficiently effective?
> **Therapeutic costs** – will the overall cost of care be lessened by the new treatment?
> **Symptoms** – how do the symptoms impact the quality of life for the patient? What is the impact on family as caregivers, if any?

Market penetration will be assumed to be 100% (i.e., all individuals meeting FDA label requirements for treatment will be treated) unless modified in this section of the worksheet. Modification of the percent of patients seeking treatment will adjust the plan specific incidence and prevalence rates.

Step 2: Uptake/adoption curve adjustment

The product uptake or adoption curve reflects how quickly patients likely to be treated will be treated. The default assumption is that 100% of likely to be treated patients are treated each year. Step 2 in the worksheet allows the user to alter that assumption and adjust for local market conditions that may impact the speed of uptake such as payer coverage decisions, provider availability, local market access, etc.

When applying the worksheet default assumption of 100% treated, only newly diagnosed patients will be treated in subsequent years. Alternatively, users may customize a ramp up rate of treatment by indicating the percentage of incident patients that will be treated each year until 100% of the market penetration rate is met. Incident patients that are not treated in the year of diagnosis are added to the prevalent population. Users set the treatment rate of the pool of prevalent patients by defining the number of years it would take to treatment the entire prevalent population. Modification may be made to the number of individuals remaining eligible in the prevalent pool year to year. Diseases with high mortality rates would be one reason to modify the individuals remaining untreated in the prevalent pool to less than 100%.

Therapy Impact Modeling Tool

The Therapy Impact Model leverages the information from the Population Estimator and Market Adjustment Tools to provide the potential financial impact of the selected therapy on the user's business. It lays out a) the estimated cost of therapy in aggregate and PMPM by year, b) the "likely

maximum cost" at the 5% and 95% model intervals, and c) the cost of treating one patient (important for smaller plans infrequently having a patient).

Step 1: Therapy cost assumptions

Step 1 of the model addresses cost inputs. Users may assess the costs of the therapy alone or may bring in additional considerations such as additional costs, cost offsets and contract related adjustments.

Product cost: The default for product cost depends on the model's assignment of the product into one of seven therapeutic categories. The costs for each category are based on observations of current market prices where possible. If no existing cell and gene therapy comparable exist, the price of existing treatments adjusted for durability have been used. Default category pricing is provided in Table 2. Users may override the default cost assigned.

Table 2 Default price points for therapy impact modeling

Therapeutic Category	Price per Patient Treated
Ultra-orphan	$1,500,000
Orphan	$800,000
Ophthalmological (genetic)	$800,000
High Prevalence	$500,000
CAR-T/TCR	$400,000
Ophthalmological (non-genetic)	$100,000
Osteoarthritis	$50,000

Associated costs: Expanding the financial impact of a new cell or gene therapy are the associated costs. Potential costs include pre-therapy preparation and work up, post therapy care, travel costs, etc.

Contract related adjustments: Payer cost of the therapy may potentially be offset by various contract arrangements. Such offsets include rebates and secondary insurance (stop loss or reinsurance) payments. The modeling tool provides an area for entering funds that offset costs. How the timing of offset payments impact financial management of costs should be considered.

Step 2: Financial risk assessment

This section of the worksheet will provide the annual cost of therapy in aggregate and as a per member per month (PMPM) cost based on the adoption rate and cost assumptions entered into the model. The 95th percentile of patient volumes, therapy costs and PMPM impact is reported to illustrate the "likely maximum cost". Finally, the cost of treating one patient (important for smaller plans infrequently having a patient) is presented as total cost and PMPM impact for the plan.

The variability in patient volumes and corresponding financial impacts will vary with the disease incidence and prevalence. Results within the worksheet can be frozen to an even distribution of lives. The worksheet is set up to also recalculate the values to give insight into the likely range of actuarial volatility.

Solution Prioritization Tool

The Solution Prioritization Tool is intended as an aide to narrowing the precision financing solutions identified by the FoCUS Consortium for addressing different financing risks. It asks you to consider the expected financial therapy impact and your organization's preferences in management of the cost. Based on the assessment choices made, the Solution Prioritization Tool will suggest potential preferred financing solutions.

Step 1: Payer financial assessment

Questions are provided to consider the three key areas of risk for cell and gene therapy – Actuarial, Payment Timing, and Performance. Recording of yes or no responses to the questions aids in capturing concerns for user's simultaneous consideration of the organization's perspective of risk.

Step 2: Needs determination and potential solutions

Building on considerations of step 1, the three questions in step 2 will drive the recommendation of potential financial models that fit the organization's cost management strategy for the selected gene or cell therapy.

The financial solutions are listed on a table that adds considerations for the implementation of each solution. Internal capabilities may or may not be present within an organization to move forward with the potential solution. Building these capabilities internally may not be efficient for all payer organizations to serve patients or to establish contracts with treating providers and developers. Market solutions are emerging to efficiently address the required capabilities. Based on the service required, FoCUS has created a Supplier Evaluation template to aid in obtaining that service.