Company

Planning Guide for Institutional Access

This guide provides our team members with a background in how decision-making processes are generally structured in children's hospitals.

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Questions contained in these call outs are designed to initiate an analysis of your account. Additional questions and space to capture your answers is provided in your companion guide.

Background

The institutional environment can be organizationally complex with many decision-making processes and a multitude of competing priorities, all of which will vary among institutions. Facilitating patients' access to the Product requires an understanding of the processes and stakeholders engaged in making the decision to offer the Product at each institution. CLN2 patients progress rapidly; in order to offer the Product to these at-risk patients, we want to help accelerate institutions' planning processes through providing information and assistance to each institution as they determine whether and how to offer the treatment.

Treatment planning processes are equally important; the Product is not necessarily a complex treatment to administer, but several characteristics make it different from other infused treatments. We need to ensure that provider teams have access to the information needed to understand the Product's unique requirements and develop effective treatment plans. A well-organized and efficient approach to treatment planning is also expected to improve patient safety and the family's experience.

This guide provides our team members with a background in how decision-making processes are generally structured in children's hospitals. It identifies key processes and notes the types of decisions made in each, as well as the stakeholders likely to be involved in each process. We also provide a set of tools and templates that our Account Managers (IAMs) may choose to share with provider stakeholders during live discussions. These tools and templates are meant to be illustrative, not prescriptive, and to help providers think through the preparation needed to successfully offer the Product to the eligible CLN2 patients in their institutions. This guide focuses on the key early steps around deciding whether to offer the Product and will assist institutions in developing treatment plans. Once an institution administers its first treatment, the institution's internal quality and review processes will engage.

Intrathecal administration is a route of administration for drugs via an injection to the **subarachnoid space** so it reaches the cerebrospinal fluid (CSF) at any level of the cerebrospinal axis. Including: 1) the cerebral ventricles (referred to as intraventricular ointracerebroventricular (or ICV), 2) into the spinal canal (referred to intrathecal lumbar).

Most new drugs are not subject to this level of scrutiny. The Product differs from "normal" drugs in multiple important characteristics, including route of administration, duration of each treatment, and the need for post-treatment monitoring. We want to ensure that these differences are understood and their implications are clear to the institutions. Examples of specific differences include the requirements inherent in intraventricular administration, including:

- Coordination of roles and coverage between neurosurgery for port implantation and the attending neurologist or geneticist for ongoing administration of the Product
- Training in intraventricular administration procedures for MDs, RNs and RNPs participating on the care team

Process Phases

We've summarized provider institutions' adoption and treatment planning processes into four distinct phases. The phases, key activities, and their proposed sequence are illustrated in Figure 1.

FIGURE 1:
PLANNING AND IMPLEMENTATION FOR THE PRODUCT

Deciding to offer a new treatment

Institutional process for electing to offer treatment to patients based on:

- Organizational priorities
- Clinical value proposition
- Economic considerations

Planning to treat initial patient

Developing detailed plans including:

- Site of care
- Skill mixes
- Training
- Protocol development
- IT
- Pharmacy and patient logistics
- Contingency planning

Initiating treatment

Implementing the plans

- Patient selection criteria
- Provider training and education
- Implementing treatment protocols
- Reviewing and modifying as needed

Continuing biweekly treatment

- Establish routine scheduling to accommodate product dosing schedule and patient conditions
- Collect/monitor longitudinal data

Four topics for all phases:

Clinical
Financial
Operational
Patient/Family

Our guide discusses the process in detail by examining four topics common to all phases.

- Clinical topics include criteria for treatment and development of standard operating procedures, site of care selection, staffing requirements, training, and credentialing (if necessary)
- Financial topics primarily address costs of providing treatment and the process for determining an amount of reimbursement for both the port installation and subsequent treatments
- Operational topics focus on the availability of resources and executing plans through scheduling, training, ordering of supplies and the Product, and delivering the prepared drug to the patient's bed or other treatment site
- Patient and family topics revolve around ensuring that families understand the benefits and risks of treatment and have the ability to comply with the requirements of biweekly treatment

Decision To Offer The Product

Our partner organizations are sophisticated and capable institutions with extensive resources. However, demand for resources frequently outstrips supply and institutions are continually forced to make tough decisions to ensure that their people, facilities, and financial resources are efficiently allocated consistent with their missions. An institution's decision to offer the Product will require consideration of a process that shares many commonalities across institutions.

What specific structures and features make this institution ideal to adopt the Product?

Process for Deciding

Whom have you identified as your institutional physician advocate?

A strong physician advocate is absolutely critical to an institution's decision to offer the Product. Advocates must have the skills and level of influence required to initiate the adoption process and shepherd the process through to offer the Product.

Most institutions will rely upon a multidisciplinary team to assess the Product's adoption through a comprehensive examination of patients' unmet needs, the Product's safety and effectiveness, resource requirements for administration, and financial considerations. These assessments may be completed in the form of a standard Pharmacy and Therapeutics assessment, together with a business case that may be reviewed by senior management.

During this process, we expect that a team including representatives from a wide variety of stakeholder groups will participate at some level. Table 1 provides a view of these groups. Note that each institution will have its own mix and may include one or more groups not listed here.

A strong physician advocate is absolutely critical to an institution's decision to offer the Product.

TABLE 1:
STAKEHOLDER GROUPS REPRESENTED IN DECISION PROCESS

Physicians	Non-Physician Providers	Administrative	Operational/ Technical
• **Genetics***	• Inpatient Nursing	• Ambulatory Care	• Potential role for representative from COO's office
• **Neurology/ Neuroscience***	• Outpatient Nursing	• Finance and/ or Strategic Planning or Operational Planning	
• Neurosurgery	• Advanced Practice Nursing	• Nursing Administration	
• Pediatric Intensive Care	• Pharmacy	• P&T Committee	
• Hematology/ Oncology			

**Physicians in Pediatric Neurology or Genetics are the most likely Product advocates and are likely to oversee the decision process, with support from the other groups listed*

The Pharmacy and Therapeutics Committee (P&T) will frequently make an initial decision to accept or reject the Product based upon clinical and non-clinical aspects. A subsequent business case may be constructed following the P&T decision, and then reviewed by an ad hoc committee of senior administrators who will consider the clinical and financial aspects prior to making a final decision. A business plan is very likely to be required in situations where reimbursement is uncertain.

Who are the members of the P&T Committee that will be involved in the review of the Product?

Clinical Assessment: Assess the unmet need and impact of providing the Product

The P&T committee or similar group focuses on determining the Product's clinical value proposition in the context of their institution's priorities and mission. A monograph or other form of assessment will be developed, nearly always by a clinical pharmacist. Figure 2 is abstracted from The American Society of Health System Pharmacists' recommended assessment approach and identifies key sections of a P&T review. The Company's information packages will contain many of the items required, but providing others may require a referral to Medical Affairs.

Has the clinical pharmacist been identified?

FIGURE 2: DRUG EVALUATION ASSESSMENT COMPONENT

- ☑ Brand and generic name
- ☑ FDA approval date
- ☑ Pharmacology and mechanism of action
- ☑ FDA-approved indications
- ☑ Dosage forms and strengths
- ☑ Recommended dosage regimens and administration
- ☑ Pharmacokinetic considerations
- ☑ Use in special populations (eg young children)
- ☑ Pregnancy category and use during breastfeeding
- ☑ Data on efficacy; in the case of the Product, this will be absolute efficacy, as no alternative treatments exist
- ☑ Clinical trial analysis and critique
- ☑ Medication safety assessment and recommendations; adverse events, drug-drug, and drug-food interactions; specific therapy monitoring requirements, administration topics, storage and stability requirements; potential for medication errors
- ☑ Financial analysis, including acquisition costs and budget impact

Source: American Society of Health System Pharmacists

We need to support this process and, to the extent possible, ensure that the information used and the interpretation of the data are correct. We have a responsibility to ensure that the information is not misleading, and that risk information is presented alongside efficacy information. Some of the information from the P&T Committee's assessment will flow into the subsequent business plan; inaccuracies or misunderstandings can thus emerge as problems in the business case, which will ultimately be reviewed by senior managers within the institutions.

What steps will you take with the clinical pharmacist and other members of the P&T Committee to ensure they understand the Product's clinical value proposition?

Financial: Determine the business case for offering the Product

Finance, Strategic Planning, or Business Development groups are likely to be recruited to develop a comprehensive analysis of costs and revenues for the new treatment. Business plans examine unusual and high-cost new treatments from the lens of patient needs, the fit with the institution's mission, resource requirements, and financial viability. The plan may focus primarily on financial issues or may be more comprehensive, including assessments of all current resources and their suitability for use with providing the Product. The Company can assist with this analysis by providing a data set of payer information and categories of resources we anticipate institutions will require. An example outline for a business case is provided in Figure 3.

The Company can assist with business plan analysis by providing a data set of payer information and categories of resources.

FIGURE 3 BUSINESS PLAN OUTLINE

1. Executive Summary: Brief description of unmet need, fit with institution's mission, and operational and financial considerations, including incremental hiring and capital needs
2. Rationale: Description of the unmet need and institution's unique ability to serve based on medical staff and current patients; role in advancing mission and strategic goals
3. Program's Patient Population: Number of patients expected to be served in terms of new starts and continuing patients vs. patients repatriated; alternative treatment sites and competitors
4. Operational Requirements:
    a. Organizational structure for team assigned to new treatment
    b. Staffing: Existing and new hires for medical, pharmacy, and nursing staff
    c. Training and credentialing needs for MDs and nursing staff
    d. Facilities: Site(s) of care; resource needs vs. availability for expected patient volume for beds, lab, radiology, and pharmacy
    e. Equipment: Refrigeration and other pharmacy requirements; pump provision and maintenance
    f. IT systems requirements and plan; may include entering treatment plans into Electronic Medical Records (EMRs)
    g. Quality planning
5. Financial Analysis
    a. Startup costs, including capital equipment, hiring and training, facilities expansion
    b. Operating costs
    c. Anticipated payer mix and reimbursement, including contracting needs, cost recovery, and patient out-of-pocket costs
    d. Cash flow from program
6. Regulatory requirements
7. Time line for implementation
8. Feasibility: Risk assessment for staff; facility resource constraints; government regulations; payer actions

Source: Synthesized from Massachusetts General and Advisory Board business plan templates

What resources will you use to uncover this key information from your account?

The actual work of pulling together the information and analysis will probably be assigned to a manager or director in the institution's finance, strategic planning, or operational planning group. A committee of stakeholders ought to be convened in order to establish a clear accountability for the plan's development and findings, and to provide linkages to key individuals in other parts of the institution.

Key analyses in the Business Plan will include:

- Estimated payer mix. Note that patients with commercial insurance, and who are "in network," are likely to be fully reimbursed per contract terms
- Projected setup and ongoing costs. One-time setup costs may include designating and training staff, purchasing equipment (eg, infusion pumps), negotiating payer contracts, and facility modifications. Ongoing costs will include staffing, drug acquisition and preparation, supplies, the overhead costs associated with potential sites of care, and administrative overhead
- Assessment of reimbursement adequacy in various potential sites of care, possible reimbursement shortfalls, and remedies. An institution's ability to assess reimbursement will be complex for multiple reasons:
  - Site of care uncertainties. Reimbursement varies based upon whether the patient is treated on an inpatient or outpatient basis. Hybrid approaches, eg "23-hour observation stays," offer additional options, but also increase the complexity of calculating expected reimbursement. Additionally, individual patient needs may impact the choice of treatment location and duration. It is important to remember that selecting the site(s) of care is each institution's independent decision

What resources will you share with this institution about reimbursement support?

  - Each institution will have a variety of arrangements with its payers, adding complexity to this analysis. We expect that many institutions will need to negotiate "one-off" contracts with payers for many patients
  - Payer approaches and levels of reimbursement methodologies differ substantially. Some payers, including Medicaid, may reimburse less than the actual cost of care
    - Inpatient care is likely to be reimbursed through a flat payment for all care in the form of a DRG or APR-DRG, or a flat daily rate in the form of a per diem
    - Care classified as "outpatient" frequently reimburses the cost of services and supplies separately from the cost of the Product, leading to improved recovery of costs
    - Certain children's hospitals are capitated for at least some share of their patients. In these cases, all cost of treatment will be absorbed by the institution or its risk-holding subsidiary
    - In all cases, billing and coding decisions are determined solely by each institution
- Resource availability is a critical part of the business plan, as many institutions enjoy high utilization of inpatient and outpatient units and employ staffing models that ensure little slack among the nursing and pharmacy staff. Inpatient sites will be a particular challenge for institutions that normally operate with a high average daily census

Operational: Compare treatment requirements to existing resources, including equipment, IT, and physician and nursing staff

The Product administration requires that specific equipment and provider resources are available to ensure successful patient "onboarding" and provision of chronic treatment over a period of years. These will vary among institutions and will typically include specific personnel, such as neurosurgeons, pediatric neurologists, specially-trained nurse practitioners or physician assistants, and other physician resources. Institutions will differ in their planned staffing models and skill mix as well as their choice of site of care, but all will need to address several common staffing needs during this decision process:

- Meeting training and credentialing requirements for nursing staff and, potentially, physicians
- Scheduling adequate staff resources to provide biweekly treatments to the projected number of patients
- Potentially hiring additional qualified staff to provide the Product treatment or backfill existing staff selected to do so. Hiring plans can present a major hurdle to the decision to offer the Product

What processes have your institutions used when adopting novel treatments?

Institutional experience with patients receiving treatments via intraventricular or intrathecal routes of administration, or biweekly treatments of more than 4 hours, is a convenient source of information for this process. This type of experience may exist in departments including neurosurgery and hematology/oncology, or in separate neuro-oncology sections.

Our partner institutions will assess their ability to provide services to a projected number of patients, or may elect to limit the number of patients treated depending upon their resources and priorities.

Institutions will differ in their planned staffing models and skill mix... but all will need to address several common staffing needs during this decision process.

Tap here to see an example of how an institution may adopt a novel treatment.

Family and Patient: Identify support and educational requirements

A comprehensive assessment will include the patient and family needs.

- Education needs regarding what to expect from treatment and how the treatment process will flow
- Assessing families' potential social and logistical needs, including transportation and lodging during the biweekly treatment protocol

The Company's Role

The Company personnel are responsible for securing the site's decision to offer the Product through providing information and support where needed to achieve this outcome.

IAMs and Medical Affairs can support institutions' decision processes by providing factual and balanced product information regarding effectiveness; drug administration, handling, and preparation; and safety, always remembering that each institution will arrive at its own decisions independently.

The minimum information provided should include:

- The package insert information, including supplies requirements and quantities, DME requirements and administration instructions (consistent with PI)
- The Product's AMCP dossier may be provided by Medical Affairs if an unsolicited request is received
- WAC pricing information for the Product may be provided by Customer Service
- Information on the Company Special service offerings for CLN2 patients, and relevant advocacy groups and foundations
- Epidemiology, including estimated treatable prevalence and potential duration of therapy

What is your strategy to build strong connections with your Company counterparts to ensure effective account management within your institution?

TABLE 2: INSTITUTIONAL ROLES, RESPONSIBILITIES AND ACCOUNTABILITIES: DECISION TO OFFER PROCESS

Role	Organization/Department/Function
Responsible: Individuals or teams assigned to complete the assessments	Pharmacy for P&T Strategic planning, operational planning, or finance for business plan analysis and process management Nursing administration, or operations in the form of nursing administration Neurology and/or genetics MDs
Accountable: The individual answerable for accuracy and sufficiency of assessments	MD advocate or leader of assessment team Pharmacist for P&T assessment
Consulted: Subject-matter experts providing information to assist process	Wide range and will vary by institution. Expect pharmacy, neurology, genetics, neurosurgery, nursing administration, PICU MD, nursing, and PICU unit manager Hematology/oncology MDs and nurses, possibly pharmacy Ambulatory care administration The Company–product information
Informed: Other stakeholders who are informed of process and outcomes, usually at beginning and completion of process	Senior administrators and probably relevant department chairs The Company Patient families

In your institution, do these stakeholders and departments collaborate? When do these stakeholders and departments collaborate? How can you create an opportunity to unify the decision makers?

Planning For Treatment

Process for Planning

Once the decision to offer the Product has been made, institutions will begin making plans to treat the first patient. Planning teams will include many of the same stakeholders who participated in the Offer Process, but should expand to include additional operational and clinical individuals. Roles will also evolve as individuals who earlier only provided information now move to assume responsibility for designing treatment and logistical processes. Table 3 provides a view of the stakeholder groups involved in treatment planning. Groups may vary by institution and it is important for the IAMs to understand who may be involved to track and encourage progress.

TABLE 3: STAKEHOLDER GROUPS PARTICIPATING IN TREATMENT PLANNING

Physicians	Non-Physician Providers	Administrative	Operational/ Technical
• Genetics • Neurology/ Neuroscience • Neurosurgery • Pediatric Intensive Care • Hematology/ Oncology (if H/O provides infusion services)	• Inpatient Nursing • Outpatient Nursing • Advanced Practice Nursing • Child Life (inpatient only) • Pharmacy • Nursing coordinators/ case managers (may be titled "navigators") • Social Services	• Admitting • Ambulatory Care Management • Pediatric Intensive Care Unit Management • Patient Accounting • Quality	• Biomedical Engineering • IT • Materials Management/ Pharmacy Purchasing

Plans need to be developed to address each step in a patient's journey.

Plans need to be developed to address each step in a patient's journey- from confirming the diagnosis, to assuring eligibility for treatment with the Product, to installing the Ommaya reservoir, and through routine biweekly treatment. While a single, multidisciplinary team is likely to coordinate plans, individuals or sub-teams from these stakeholder groups will be responsible for completing plans for their own organizations and ensuring that their plans coordinate with those of the other groups'. Table 4 presents a checklist of topics that should be addressed during the planning activities.

Which member of the patient care team is responsible for developing this plan?

TABLE 4: PLANNING CHECKLIST

Patient Onboarding	Medical Center Resources	Regulatory Requirements	Administrative/ Financial Topics

• Number seeking treatment
• Physical status; eligibility for treatment
• Financial and Logistical Needs Assessment
• Individual treatment plan established in EMR
	• Physicians; Neurosurgery, Neurology, Genetics (?)
	• Nursing
	• Pharmacy
	• Patient Navigators/ Coordinators
	• Equipment
	• Supplies
	• Facilities
		• Training and credentialing needs
		  • Physicians
		  • RN/RNP/PA
		  • Pharmacists
			• Facility requirements
			• Prior authorization
			• Reimbursement
			• Coding
			• Payer contracting
			• Payer Network
			• Out of state Medicaid

Clinical: Clinical planning addresses the actual "how to" for developing the patients' treatment plans

Figure 4 provides a highly simplified flow for the clinical planning process. We include a more detailed treatment flowchart for the Treatment Planning section in Figure 5 and a useful template for planning logistics activities in Figure 6.

FIGURE 4: PROCESS FOR TREATMENT PLANNING

Once your institution has decided to use the Product, how will you initiate these three steps?

Patient Onboarding

The clinical plan defines each patient's eligibility for treatment. This may be based upon either the institution's criteria or payer criteria and is likely to consider the Product's FDA-approved indication. The clinical trial's inclusion and exclusion criteria may influence eligibility definitions for some institutions.

- Patients' eligibility may be established through institutional criteria, but these may also need to accommodate payers' coverage requirements, including potentially both TPP1 status and an acceptable score on the CLN2 Rating Scale in order to gain reimbursement
- Note that providers will need to be trained on using the CLN2 Rating Scale and in documenting the results both during patient onboarding and on a regular schedule once treatment begins
- Each patient's treatment plan will need to be developed and entered into

the institutions' electronic medical record or computerized physician order entry system (CPOE) to ensure coordination and scheduling of resources

A confirmed diagnosis and completed baseline testing (as part of the patient onboarding processes) will serve both to confirm the patient's clinical eligibility for treatment and provide documentation likely required to secure reimbursement. Baseline testing is likely to include:

- Laboratory diagnostics including blood and cerebrospinal fluid tests and MRI (potentially) must be identified and built into the onboarding flow
- Functional measurements must be collected during the initial patient encounter as well as closer to the first treatment date. Note that patient progression between the testing date and treatment initiation is increasingly likely as the amount of time increases. Each payer's requirements for pre-treatment testing may need to be clarified
- Payers may also require a recertification of patients' eligibility on a regular schedule, possibly as frequently as twice per year.

Treatment Planning

The intraventricular infusion team will be identified, and requirements will be translated into a specific training and credentialing program for the physicians, nurse practitioners and/or physician assistants who will administer the Product and monitor the patient during and after the 4.5 hour infusion. These providers will likely also be responsible for ensuring that patient's physical condition is adequate to receive treatments.

Has this institution identified a location where the Product can be administered and monitored for at least 4.5 hours?

The initial treatment protocol will be delineated, including installation of the Ommaya reservoir, timing of first infusion post-surgery, and identifying sites of care and the infusion team responsible for first and subsequent infusions.

Key topics to consider as treatment planning progresses include:

Time lines will be important to address in the treatment plan. Many institutions provide straightforward infusion therapies on a chronic basis, or more acute treatments on a short-term basis, but the Product represents a resource-intensive treatment that will be provided biweekly for years in sites of care which are not typically used for repetitive treatment.

- Scheduling of resources is a critical step in treatment planning; for example, one institution reported having PICU bed availability for the Product patients on Mondays only, prior to surgical cases being admitted on Tuesdays and Wednesdays
- Patient lab work may vary, with some institutions conducting lab work on treatment days and others potentially requiring patients to have lab work

The Product represents a resource-intensive treatment that will be provided biweekly for years in sites of care which are not typically used for repetitive treatment.

completed at some time prior to each treatment

- Strategies for procuring the Product may also differ, depending on the number of patients receiving treatment at each institution and the Product's distribution strategy
  - Institutions with multiple active patients may elect to keep 1-2 treatments in stock while those with a single patient may prefer to order each treatment separately as needed
  - Delivery times will vary according to distribution. Drop-shipping may require ordering 3-4 days in advance of a treatment while distribution by the institution's wholesaler may allow ordering the day before each treatment

What is your institution's materials management process for handling special products of this nature?

Physician roles in the first infusion must be articulated, particularly the degree of engagement for the neurosurgeon and pediatric neurologist. The neurosurgeon may want to attend or even administer the first intraventricular infusion but then move to "on call" status for subsequent infusions. Alternatively, a pediatric neurologist may choose to first access the port and start all infusions for some period of time as experience with the treatment and patients accrues.

Pre-Medication(s). Timing and assigned responsibility for administering patients' pre-medication(s); these may initially be administered in the hospital, but parents may be assigned responsibility as treatment becomes routine.

Drug stability is an important requirement to consider during this planning process; the Product's stability in a syringe is currently confirmed for 8 hours. Thus, a process that calls for early syringe preparation and then trundles ahead at a slow pace may result in the Product "timing out" should the treatment not be completed within 8 hours of syringe preparation. Some institutions may prefer to not defrost the Product vials or prepare syringes until after a patient is in the facility with confirmed eligibility for each treatment.

The Product's stability in a syringe is currently confirmed for 8 hours.

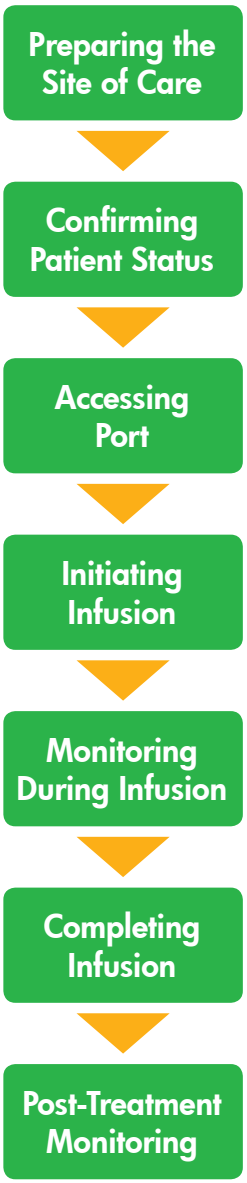
Does this institution have freezer space available in a freezer capable of storing the Product at -25 to -15 centigrade?

A resuscitation plan for responding to potential adverse events and other emergencies during treatment or during post-treatment monitoring must be developed and remain active during the time the patient is in the hospital. Clear instructions on which MD(s) to call if an AE emerges are required. This is likely to be the attending PICU physician while the patient is in the PICU, but may include additional physicians and clinical pharmacists. A resuscitation plan will be more complex if the site of care is outside the PICU, in which case a designated team (likely pre-existing) will be identified and must be trained to understand the patient's condition and treatment.

Figure 5 provides a high-level treatment flow process. Key decisions to be

made within each step of this flow include skill mixes, sites of care, and scheduling coordination for port installation and first treatment.

FIGURE 5: TREATMENT FLOW PROCESS



Preparing the site of care: Logistics will vary among institutions and also among sites of care, but in general the treatment room must support the institution's sterility requirements, provide adequate accommodation for the accompanying parent, and allow for either instrumentation or direct monitoring by the RNP and physicians. Supplies, including the infusion pump and spare tubing and needles, may be pre-positioned in the room.

Confirming patient status: Pre-treatment checks will be defined for ensuring that patient's physical condition is adequate.

- At a minimum, providers will be encouraged to perform an assessment using the CLN2 Rating Scale on a regular schedule; a CT or other diagnostic radiological exam may also be required to confirm the Ommaya reservoir and catheter's status prior to the first treatment
- Criteria for proceeding or delaying treatment will be defined as part of the protocol
- Parents may need to be trained to identify situations requiring postponement of a treatment along with the correct provider to contact

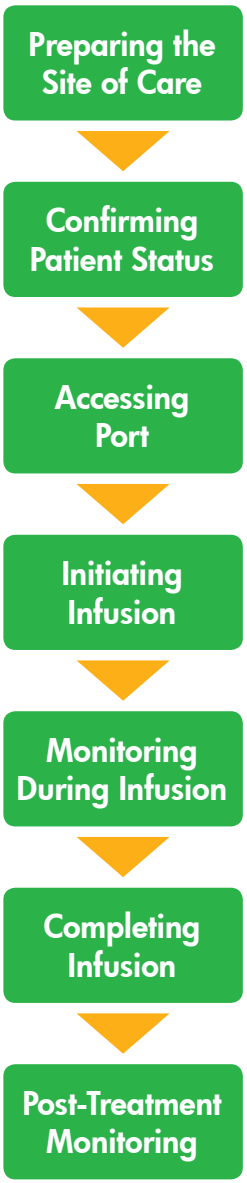
Accessing the port: Each institution will determine the appropriate skill mix for inserting the needle into the Ommaya reservoir. Provider opinions varied during site visits, but we heard general agreement that either a pediatric neurologist or an RNP would be trained and credentialed for this task.

- Patient restraint during needle insertion is a key topic for planning as head movement or resistance to treatment complicate the procedure. As personnel's availability may change for a wide variety of reasons, institutions should have several individuals trained and certified for completing port access
- Some institutions may include a requirement to withdraw a small volume of cerebral spinal fluid to confirm the port's patency and for testing purposes
- Providers may be encouraged to develop a tactic for securing the needle in the port during the infusion, bearing in mind the patient's age and response to treatment

The implementation protocol should be developed prior to the first treatment

Initiating the infusion includes multiple steps including confirming the pump's programming; confirming the medication; inserting the syringe into the pump; and beginning the infusion. Note that some institutions may prefer to accomplish some or all of these tasks prior to accessing the port. Steps required to secure the patient and the infusion tubing may be specified during protocol development

FIGURE 5: TREATMENT FLOW PROCESS



What experience does this institution have with intraventricular drug administration?

Monitoring requirements during the infusion: Institutions may vary in their monitoring requirements, and these requirements may evolve as experience with patients and the Product accrues. Interviews suggest that patient's vital signs should be constantly monitored if initially treated in a PICU, and that the patient will be under frequent, if not continuous, observation by an RNP. For patients treated outside a PICU, the treatment plan should identify the frequency of checking vital signs and the degree to which monitoring must be continuous or at defined intervals

- Patient management during the treatment requires planning and should allow for multiple options, as patients' tolerance for remaining in a bed for long periods of time will probably vary substantially

Completing the infusion: Once the syringe is empty, the provider must remove the Product's syringe from the pump and replace it with a syringe containing the intraventricular solution provided in order to ensure that the the Product remaining in the tubes, Ommaya reservoir, and catheter are pushed completely through and into the ventricle. The treatment plan must identify the specific steps and quality checks required to replace the Product syringe and complete the treatment. At the conclusion of the treatment, the needle must be removed from the port. Vital signs and other status measures should be recorded in the treatment record, likely in the EMR

What educational materials or support could you provide this institution to increase their comfort level with this novel treatment approach?

Post-treatment monitoring: Specific plans will include the steps taken to secure the patient and ensure that a safe level of monitoring continues over a time period selected by the institution.

- Institutions will determine the duration of post-treatment monitoring
- Skill mix and site of care may differ from the treatment choices for the monitoring period
- Accompanying parents must also be accommodated and may play a formal role in monitoring the patient

Logistics

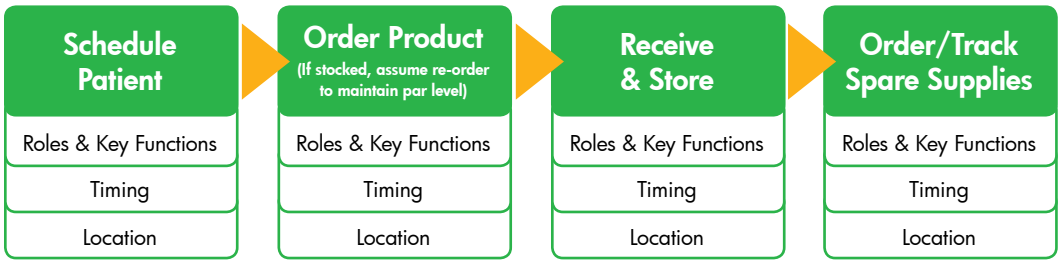
Protocols will need to be implemented as order sets and therapy plans in the institution's EMR and/or order entry systems to ensure that the protocol determined by the planning group is implemented correctly and to support resource scheduling and data collection

What EHR system does this institution use, and who is the stakeholder responsible for managing the system?

- Order sets will be developed which specify the equipment and supplies needed for each treatment, as well as generate lab test orders and trigger room and provider scheduling
- A data collection and analysis plan should be established during the treatment planning process in order to acquire the longitudinal data needed to support safety/outcomes studies, and to inform the institution's quality improvement process
- Ordering the Product and ensuring that the treatment and associated supplies are available will vary among institutions. Figure 6 provides a high-level view of the process flow and provides a template for understanding how each institution may approach this task.

The availability of the treatment and associated supplies will vary among institutions.

FIGURE 6: LOGISTICS FLOW FOR THE PRODUCT



Financial planning: Focus on reimbursement issues and resource consumption

Financial planning includes general tasks of cost and reimbursement estimation common to all patients and new treatments, including determining correct procedure coding and billing for both inpatient and outpatient sites of care. Individual-level planning will also occur, but will primarily focus on reimbursement topics. Tasks included in the financial planning process will include:

- Estimating cost of care per patient. This analysis may be a simple update of the analysis performed for the business plan and should include installation of the Ommaya reservoir and catheter, and a cost per intraventricular treatment, potentially for multiple sites of care within the institution
- Determining reimbursement and ensuring that any potential shortfalls of reimbursement are estimated and planned for, with potential assistance from alternative funding sources
- Nurse coordinators or case managers and/or the admitting or patient accounting departments will focus on completing insurers' pre-certification and prior authorization requirements and will work with families to collect out-of-pocket costs or find sources of patient financial assistance. Gaps between reimbursement and costs will be identified and planned for by the institution and the patient
- Coding needs to be addressed in the planning process, as intraventricular infusion does not have a specific CPT procedure code. The institution may elect to bill for administration and related procedures under a "miscellaneous" procedure code
  - The institution may determine charges using their own methodology or by basing charges on analog codes
  - The Company may provide a basic guide to reimbursement (PA packet); however, childrens' hospitals are responsible for determining billing codes, completing payer forms, processing, and achieving reimbursement

Gaps between reimbursement and costs will be identified and planned for by the institution and the patient.

Has this account established guidelines on how to bill for this type of procedure? Who will be responsible for coding these claims at this institution?

- The institution may have one or more patients for whom the hospital is "out of network" for a commercial payer, resulting in potentially very high out-of-pocket costs for the patients' families. In these cases, the hospital will seek to negotiate a specific "one-off" contract with the responsible plans for each patient
  - The negotiation is most likely to involve the Chief Financial Officer or a manager from the Managed Care/Payer Relations department
  - Similar negotiations may be required for patients covered by an out-of-state Medicaid agency
  - The group charged with concluding these negotiations will ideally have a thorough analysis of treatment costs available prior to beginning the negotiation. The Company's data demonstrating outcomes can support these negotiations by providing clinical data to demonstrate the Product's value
  - Hospitals may be unable to waive coinsurance payments without violating payer contracts, leaving the choice of either treating these payments as "uncollectables" following some attempt at collection, or finding alternative funding sources

Operational plans: Focus on ensuring that the facilities, supplies, and equipment are available for treating CLN2 patients

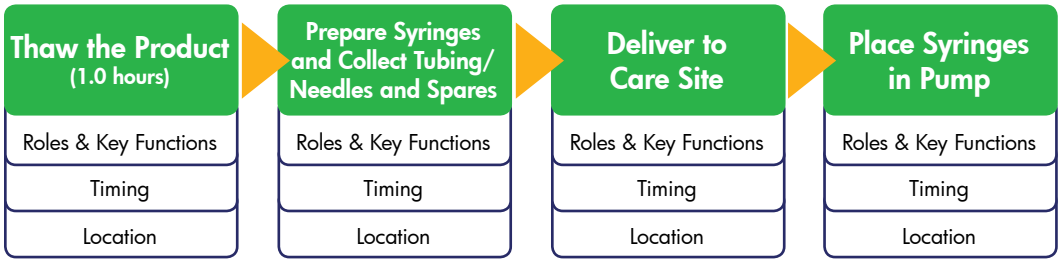
Pharmacy

The Product must be stored at between -25 and -15 degrees centigrade, and stability following defrosting and drawing into a syringe is certified for 8 hours. While pharmacy operations in our centers of excellence are sophisticated and accustomed to managing complex therapies, the Product's storage requirements, stability window, and the need for backup supplies require some thought and planning.

Pharmacy will establish a plan for ordering and storing vials and supplies. The process for preparing syringes of the Product and the intraventricular solution, should include consultation with Nursing. Most pharmacies will also establish a plan to ensure availability of the preferred infusion pump and spare supplies, in particular needles and tubing, close to the patient during treatment.

Figure 7 below provides an overview of how the process may likely work for preparing the syringes. The figure outlines the steps and can help raise awareness of timing and need for spare needles.

FIGURE 7: THE PRODUCT PREPARATION



The Product's storage requirements, stability window, and the need for backup supplies, require some thought and planning.

Site-of-Care

- Institutions may decide to use both inpatient rooms with adequate monitoring capability, and potentially, bedded rooms in an outpatient infusion clinic or procedure facility which have the capacity to accommodate the Product's 4.5-hour infusion, plus the preparation time, and desired post-treatment observation period
  - Keys to determining appropriate sites of care include the minimum provider skill set for performing pre-treatment assessments and infusion, and monitoring requirements during and following the treatment
- Site-of-care planning is critical and is likely to be very conservative for the first patient. Potential sites of care for initial treatments include pediatric intensive care units (PICU) in order to provide continuous patient monitoring for an extended period of time and rapid availability of staff should an adverse event occur requiring resuscitation

- Treatment may migrate to lower acuity inpatient or ambulatory sites as the institution gains experience and comfort with the Product
  - Challenges for existing outpatient centers such as infusion clinics and procedure facilities include:
    - Lack of familiarity with intraventricular infusion
    - Resuscitation/adverse event coverage
    - Sterility requirements (may be the same as inpatient, and the highest-priority concern is sterility of the injection site on the patient's scalp)
    - Long duration of the infusion, and the institution's requirement for post-treatment monitoring. Total time in the facility may be 5-6 hours for setup and infusion, followed by each institution's preferred observation time
    - Nurse staffing ratios for pre-treatment evaluation, setup and initiation of treatment, treatment administration, and observation
  - Infusion clinics and procedure rooms are typically staffed by RNs, and the institution may view this skill mix as inadequate for administering the Product as an intraventricular therapy

IT and Systems

IT systems are required to include order sets and treatment protocols in the hospital's HER/order entry system to ensure timely drug ordering and resource scheduling. Key activities for planning include:

- Assigning a key patient manager or point of contact responsible for coordinating scheduling of the patient and the required institutional resources
- Establish a plan for scheduling needed resources, including MDs, nursing, pump, room(s), and ordering of the Product

Family and Patient: Provide support and education

Families will most likely have heard about the Product from multiple other sources. During the process of determining a patient's clinical eligibility, the families will require more formal education on what to expect regarding treatment process and outcomes of treatment. Education around the treatment plan, including port installation, intraventricular infusion, and location and duration of treatment must be clear. Additional requirements for family engagement include:

- Identifying needs and eligibility for financial assistance. A financial plan for each patient will be developed and will identify insurance coverage, out-of-pocket costs, and plans for covering those through sources of financial assistance or hospital charity care if the family is unable to cover
- Obtaining an agreement to treat as part

Families will require more formal education on what to expect regarding treatment process and outcomes of treatment.

What examples can you provide to demonstrate the Company's dedication to the support and education of families and patients?

of this planning

- Providing access to a web-based patient educational tool that gives families and patients an overview of the onboarding process and a virtual tour of the site in which the patient will receive treatment

TABLE 5

Institutional Roles, Responsibilities, and Accountabilities:

Role	Organization/Department/Function
Responsible: Individuals or teams assigned to complete treatment plans	• Pharmacy: ordering, storage, preparation and delivery of the Product. May also supply and program pump • Nursing administration, or operations in the form of nursing administration • PICU or possibly ambulatory services for detailed treatment plan • Neurology and/or genetics MDs • Neurosurgery: Selection of Ommaya reservoir and catheter, surgical plan • Quality management/infection control: Establish quality plan, including setting key lab metrics • BioMed: Engineering for pump acquisition and maintenance • Admissions/patient accounting • Nurse case management, social worker or navigator
Accountable: The individual answerable for accuracy and sufficiency of assessments	• MD champion or administrative leader
Consulted: Subject-matter experts providing information to assist process	• Hematology/oncology MDs and nurses; possibly pharmacy • Ambulatory care administration
Informed: Other stakeholders who are informed of process and outcomes, usually at beginning and completion of process	• Department chairs • The Company

Treatment Planning

The Company's Role

The Product information provided earlier may need to be updated as extension trial information becomes available. Our team will probably need to initially meet with key institutional stakeholders to discuss topics such as storage and preparation requirements, safety experience, and other providers' experiences and approaches. A list of potential information includes:

- Updated safety information to inform site-of-care selection, potentially including other sites' strategies for sterility and monitoring during and following treatment. This may need to be provided by Medical Affairs in response to an unsolicited request
- Guidance on treatment processes including preparation of syringes, checking port patency, confirming that the patient's condition allows treatment, and pre-medication (as stated in PI)
- Suggestions regarding spare supplies; possibly provide specifications and SKUs for tubing, filter, and port access needles
- Payer information packages to support PA and appeals
  - Guidance on institution and the Company roles in completing PA/pre-certification process: Note that our centers of excellence are likely to complete most or all of the processes independently
    - Sharing information regarding gaining coverage for out-of-network patients: Consider referral to staff at other institutions with experience in this area.
- Referral to the Company Medical Information regarding questions on pump selection or any requests for information regarding non-FDA approved indications
- Information and materials to assist development of institution's patient and family education plan and materials

Discussions with stakeholders will likely include storage and preparation requirements, safety experience, and other providers' experiences and approaches.

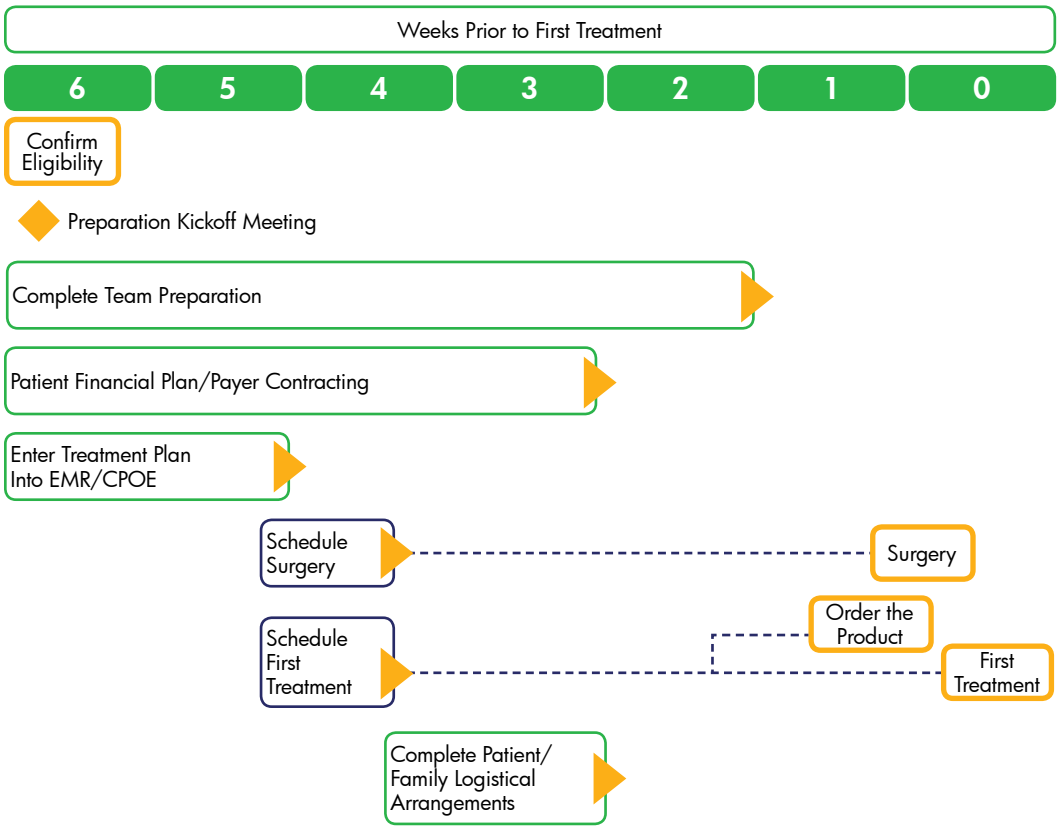
Providing An Institution's First Treatment

Onboarding and initiating treatment with the first patient includes implementation of the plans developed in earlier processes. We can expect that institutions will not begin the earlier processes until they have identified a patient who is likely to be eligible; thus the planning process should lead to implementation within a relatively short period of time. Once the first patient has been deemed eligible, we recommend a kickoff meeting to ensure that all stakeholders involved in making arrangements and providing treatment are fully apprised of the schedule and steps that need to be completed prior to administering the first treatment. The team can review the treatment plan, develop an institutional communications plan, and complete any last minute clarifications during the course of this meeting.

Implementing the detailed plans may require a minimum of 6 or more weeks and involves 5 key steps as shown below in Figure 8:

What stakeholders will you invite to this kickoff meeting? How will you lead the conversation to ensure the team has the information and support they need to create their treatment plan?

FIGURE 8: PREPARING FOR THE FIRST PATIENT



- Qualify the first patient using the institution's eligibility criteria
- Complete care team preparation: Designate a lead physician and nursing and pharmacy staff members, and complete disease education and training on the Product's administration requirements
  - Identify and complete any credentialing requirements for intraventricular infusion and management
  - Ensure sufficient provider numbers to provide coverage should one or more members of the treatment team become unavailable. Plan to ensure that designated "backups" gain and maintain familiarity with the process and with patients and families
  - Ensure and document compliance with state and institutional requirements for credentialing and training
- Finalize the patient's financial plan, including payer authorization, potential one-off contract negotiation, and estimation of patient's out-of-pocket costs
- Complete logistical planning for the patient and accompanying family members. This planning may include obtaining funding for local housing and travel expenses
- Finalize treatment plan and enter into EMR/CPOE as protocols and order sets. Once the plan is entered, the IT system will facilitate scheduling of resources (facilities, equipment, and personnel) and schedule the initial order of the Product and supplies, including spares

...expect a high level of interest and participation as (the first) patient will represent a first for the institution on a number of different levels.

A broad range of stakeholders will be engaged with arranging and providing the first patient's treatment. Many of the procedures and processes used to treat the the Product patient will be familiar to the institution; however we can expect a high level of interest and participation, as this patient will represent a first for the institution on a number of different levels. This includes introducing a new treatment for a previously un-treatable condition; potentially representing the first intraventricular patient for the institution; and the recognition that the institution is providing a high profile, unique service within its region. Table 6 below provides a comprehensive view of the providers and others who will likely engage with this first patient in some way. Note that a plan for communicating information on the new treatment to the entire institution should be complete prior to the first treatment.

TABLE 6: STAKEHOLDER GROUPS PARTICIPATING IN

PREPARATIONS FOR FIRST PATIENT

Physicians	Non-Physician Providers	Administrative	Operational/ Technical
• Genetics (tbd) • Neurology/ Neuroscience • Neurosurgery • Pediatric Intensive Care • Hematology/ Oncology (if H/O provides infusion services) • Infection Control (monitor labs)	• Inpatient Nursing • Outpatient Nursing (possibly no role initially) • Chief Nursing Officer • Nurse and MD Training • Social Services • Advanced Practice Nursing • Child Life (inpatient only) • Pharmacy • Nursing coordinators/case managers (may be titled "navigators")	• Admitting • Contracting/ Managed Care • Ambulatory Care Management • Pediatric Intensive Care • Patient Accounting • Quality • Marketing/Public Relations	• Biomedical Engineering • IT (should be complete prior to first treatment) • Materials Management/ Pharmacy Purchasing

Who are each of these key stakeholders in this institution? What is their experience in treating CLN2 patients?

The focus at this state is on implementation rather than planning–from port installation through first infusion and subsequent transition to chronic care. Approaches will vary by institution, but a kickoff meeting including key stakeholders participating in the first treatment episode is a best practice. The team reviews the treatment plan and completes last-minute clarifications in the course of this meeting.

Clinical: Patient preparation and provider training

The neurosurgeon installing the Ommaya reservoir will ensure that an appropriate device is selected and installed. Prior to the first treatment, training and education will be completed by patient care staff, including primary and backup nurses and pharmacists.

What educational materials will you use with the patient care team to ensure they are properly informed for their conversations with patients and their families?

The patient will probably visit the institution at least once prior to treatment initiation for a pre-surgical visit that will include a physical examination, imaging, and blood work. This visit provides an opportunity for the nurse coordinator (or other staff member in charge of coordinating the patient's care) to deliver an overview of the treatment and brief the family on what to expect during the surgery and subsequent treatment.

Installing the Ommaya reservoir is not inherently difficult. The patient may be kept in the hospital for 1 or 2 nights after installation of the Ommaya reservoir. The neurosurgeon responsible for installation may then pass responsibility for the patient to the pediatric neurologist after the port

is confirmed to have been successfully installed. Alternatively, the first intraventricular therapy may be started by the neurosurgeon, seeking to confirm the port's patency and suitability of the patient's physical condition to receive the first treatment.

Most or all of the nursing staff assigned to the care team are likely to attend the first treatment in order to begin gaining familiarity with the treatment and the processes, and to build their relationships with the patient and family members.

Key concerns during this initial treatment episode include:

- Surgical complications including post-operative infections and lack of patency for the installed port
- The patient's and parents' response to both the infusion process and to the Product
- The institution's ability to successfully implement the treatment and logistics plan, including pre-placement of spare supplies and successfully completing the administration protocol.

Financial: Ensuring viable cost recovery

We fully expect that all institutions will complete financial arrangements prior to the patient's admission. The arrangements will include prior authorization for both implanting the Ommaya reservoir and for subsequent treatment with the Product. Children's hospitals are among the best at achieving reimbursement for high acuity, rare conditions and our role will mostly focus on accelerating the process by providing information on the Product and general information on coding options for intraventricular administration and the Product. Figure 9 presents the outline for the Product's Prior Authorization Information Package.

Children's hospitals are among the best at achieving reimbursement for high acuity, rare conditions...

FIGURE 9: PRIOR AUTHORIZATION SUPPORT PACKAGE

1. Caveats
2. Safety Information
3. Guidance for Using this Reimbursement and Billing Guide
4. Site of Service Considerations
5. Coverage for the Product: Medical and Drug Benefits
6. Coding for Disease
7. General Coding by Site of Care and by Payer type
8. RareConnections™

Operational: Focusing on schedules and fulfillment

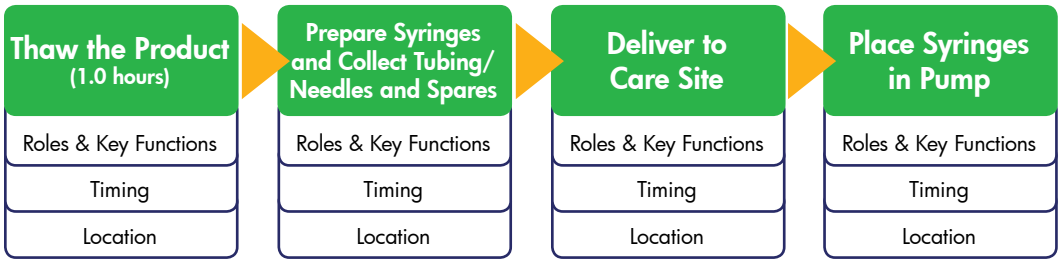
A Surgery scheduler will schedule the surgeon's time, OR time, and an inpatient room in the PICU or surgical unit for the anticipated length of stay following the implantation of the Ommaya reservoir.

Prior to the surgery date, Materials Management shall ensure that the surgeon's preferred Ommaya reservoir and catheter are available. Pharmacy or materials management will ensure that an acceptable infusion pump, spare needles, and other supplies are on hand. Biomedical engineering or pharmacy will need to program the pump and ensure that it is in working order prior to the first treatment date.

Pharmacy must order the Product and extra supplies through the institution's wholesaler prior to the scheduled date of the first treatment (see Figure 6). Spare supplies, including needles and tubing, may be pre-positioned or kitted for dispensing, along with the treatment syringes. On the day of the first treatment, Pharmacy prepares the two syringes with the Product and intraventricular solution, and dispenses to the site of care just prior to the treatment along with tubing, filter, and needles.

- Some institutions may confirm the patient's condition prior to either defrosting or drawing the Product into the syringe
- Responsibility for monitoring drug preparation and administration timing must be assigned and a process established to ensure that the Product is administered within acceptable time lines. Figure 7 provides a template for planning the steps to prepare and deliver the Product to the care site.

FIGURE 7: THE PRODUCT PREPARATION



Patient and Family: Preparing to initiate treatment

The family's logistical needs will potentially include transportation for the patient and multiple family members, if the family does not reside locally. Lodging for the patient, accompanying parent, and potentially additional family members will need to be arranged for the pre-operative checks and for any prolonged patient stay following the surgery and treatments.

Although many children's hospitals now have parent sleeping arrangements in med/surg rooms, the Product patients may be treated in the PICU, where these arrangements are less common. Regardless, the primary accompanying parent may need a nearby location for relaxation and disengagement during the first episode of care. Figure 10 provides an overview of activities and potential patient/parent activities during the first treatment.

FIGURE 10:
PATIENT AND FAMILY FLOW FOR FIRST TREATMENT

	Activities	Patient Experience	Insights
Travel	Air or car	Leaving home; facing "hassle" of travel	Minimizing distance and intensity reduces stress on patient and family
Arrival and Admission	Complete paperwork; pre-medicate	Boredom, anxiety, drowsiness from meds. Parent divides attention between child and forms	Streamlining admission procedures simplifies experience, allows parent to focus on child
Patient Prep	Gowning and draping; preparing injection site	Patient may be anxious during prep phase due to need to draw blood and shave, sterilize local area on scalp	As treatment continues, venous access may require port installation
Tests	Draw blood; access port to obtain CSF	Patient is typically distracted and/or restrained during port access; creates anxiety	Consider approaches to restraint that minimize anxiety
Treatment	intraventricular started; requires 4 hrs in bed. Withdraw needle at end	Boredom, napping. Parent and treating RNP/PA monitor child and infusion pump	Long period of time in bed; parent may require breaks; child must be comfortable with RN in place of parent
Monitoring	Child remains in bed or is transported to different site of care for monitoring	Long period of time; may be restless, need to move. Parent and child both seek diversion, sleep	Safe activities should be offered to child. If kept overnight, parent sleep setting critical
Discharge	MD or RNP meets with parent to review status, test results, confirm next date	Ready to go home. Parent and child may be fatigued, grouchy if monitoring extends overnight	A rapid and convenient discharge directly from site of care imperative
Travel	Air or car	Likely tired, anxious to get home	Minimizing intensity and time critical; parent may need to continue monitoring child

The family should have a clear understanding of the treatment plan and processes prior to both port placement and the initial the Product infusion.

A navigator or other nursing staff may find that the accompanying parent will benefit from a gentle review of the steps as the initial episode of care progresses.

The Company's Role

Our role during a patient's initial treatment focuses on providing support on an "as needed" basis, with a particular focus on financial readiness. Payers may require more time to authorize treatment than our time line (Figure 8) suggests. In cases where the institution is out of a commercial payer's network or when the patient is covered by an out-of-state Medicaid agency, a "one-off" contract may be needed, potentially causing additional delay to beginning treatment. In cases with commercial coverage, the patient's out-of-pocket cost may not be calculable for some time after the one-off contract is settled. Our IAM is on-point for providing ad hoc assistance to the institution's reimbursement staff during this time.

Provider and patient education and financial assistance should be completed weeks prior to initiation of treatment; however, we can expect delays and questions to arise as stakeholders approach their first episode of care. We need to be prepared to provide last-minute clinical information through Medical Affairs.

Continuing Treatment

Patients face 26 treatments each year, potentially for many years. Each institution will need to examine their patient's journey through the hospital and seek to streamline that journey to reduce stress and inconvenience experienced by the patient and family.

The institutions' key goal following initiation of treatment will be transitioning patients from a more resource-intensive first infusion, possibly delivered during an inpatient stay, to a sustainable and convenient biweekly schedule. Achieving this allows a patient's treatment plan to minimize the disruption to the family's routine and allows the patient to experience as normal a quality of life as possible while not receiving a treatment. This is not a Company responsibility, and progress will be based upon each institution's quality processes and staffing models, along with financial incentives and the availability of key resources, including PICU and inpatient beds as well as outpatient facility capabilities and staffing.

After your institution has successfully delivered its first treatment, what actions will you take to maintain a relationship with your key stakeholders?

Discussions of allowing additional institutions to provide treatment will also arise, as some patients' families will not live near one of our initial set of treating institutions and will want to reduce the inconvenience and expense of biweekly travel. Note that moving a patient to a new facility with no Product experience means a new institutional onboarding initiative for the Company.

Roughly the same stakeholders involved in treatment initiation will continue their engagements as the biweekly routine is established, as shown in Table 5.

TABLE 5: STAKEHOLDER GROUPS PROVIDING ONGOING TREATMENT

Physicians	Non-Physician Providers	Administrative	Operational/ Technical
• Genetics (tbd) • Neurology/ Neuroscience • Neurosurgery • Pediatric Intensive Care • Hematology/ Oncology (if H/O provides infusion services) • Infection Control (monitor labs)	• Inpatient Nursing (possibly no role after first treatment) • Outpatient Nursing (possibly no role if PICU is site for ongoing treatment) • Chief Nursing Officer • Nurse and MD Training • Social Services • Advanced Practice Nursing • Child Life (inpatient stays) • Pharmacy • Nursing coordinators/case managers (may be titled "navigators")	• Admitting • Ambulatory Care (possibly no role if site-of-care remains inpatient ward) • Pediatric Intensive Care (if remains site-of-care) • Admitting/Patient Accounting • Quality Management • Payer Contracting Department; Managed Care/ Finance	• Biomedical Engineering • IT • Materials Management/ Pharmacy Purchasing

- One or more pediatric neurologists are most likely to oversee management of the patient's care, delegating most day-to-day responsibilities–outside of treatment days–to a nurse care manager or navigator. Neurosurgery may retain a formal link with scheduling to ensure coverage should a port problem arise
- Pharmacy establishes a schedule for ordering supplies and the Product, arranging for these to be available for each treatment. As the number of patients undergoing treatment rises, pharmacy may move to stocking the Product at some par level determined by the lead pharmacist for the CLN2 program
- Advanced practice nurses may replace neurologists in administering the ongoing intraventricular treatments, strictly adhering to the established protocol
  - Institutions should consider rotating the MDs or RNPs to ensure at least several are familiar and comfortable with administering the Product through the intraventricular, as well as to build familiarity with patients and their families
- Nursing coordinators or case managers oversee the patient and family support, and provide the ongoing documentation payers may require; the nursing coordinators are likely to assume responsibility for scheduling the appropriate site of care and pre-treatment testing
- BioMed engineering maintains the institution's selected pump; given the nearly unique intraventricular time and flow rate, one or more pumps

may be permanently assigned for administering the Product

- Admitting/patient accounts tracks payments from families, payers, and organizations providing financial assistance. Renewing prior authorizations may fall to either this group or the nurse coordinators/case managers

Clinical: Focus on results and process improvement

Identifying a practical and efficient site of care is a key clinical decision in establishing the biweekly routine. Adjusting the treatment plan to fit each patient's experience is also important; for example, pre-testing procedures and observation periods may evolve as the providers gain experience with the Product and improve their understanding of how patients' pre-treatment condition impacts response to treatment.

Data detailing the treatments administered and the patient's condition must be collected and entered into a longitudinal database in order to track the Product's long-term impact on patients' conditions and also to support periodic payer recertification and inform quality program reporting.

The treatment plan should also ensure that patients' status on the CLN2 scales are tested on a regular basis that the institution will determine.

Financial: Stay up-to-date on reimbursement and coverage

Payers frequently authorize care for either 6 or 12 months. The nurse coordinators/case managers or admitting/patient accounts typically assume responsibility for ensuring that ongoing care is re-authorized in time to continue therapy with no interruptions. These individuals would also be responsible for ensuring that any clinical information regarding patient response and condition required by payers is provided.

The long, open-ended nature of the Product therapy means that families' financial resources may change over time and their ability to make cost-sharing payments may decline or improve. Patients with commercial insurance coverage may also face challenges if a parent changes employment or other events occur which threaten to interrupt coverage; for instance, if a Medicaid patient's family relocates to a different state.

The institution's admitting/patient accounts staff must be aware of any changes in a family's status that may impact coverage and full reimbursement.

Operational: Fine-tune the patient experience and resource utilization

Institutions should have a process in place for reviewing patients' experiences and adjusting treatment plans in order to minimize patients' inconvenience and the institutions' resource expenditure. Opportunities to accomplish this may include the following examples:

- Streamlining the patient intake process for each treatment, potentially admitting the patient straight to the site of care
- Broadening the team of advanced practice nurses available to provide the intraventricular infusion to reduce the impact of one or more becoming unavailable
- Adjusting physician backup requirements; for example, some institutions may require that a neurosurgeon be on call during the first several infusions, but then release that requirement as experience builds
- Selecting an outpatient clinic or procedure area in which to administer the intraventricular infusion
- Optimizing the post-treatment observation period in order to minimize the patient's time in the hospital. This may be facilitated through a combination of analyzing trial and extension safety data, training parents to observe and report problems, and providing rapid phone or Internet-based support in case the parent suspects a problem is developing.

Patient and Family: Settling in and building a routine

Patients' families will vary in their ability to adjust to the biweekly schedule. While potential stabilization of the patient's condition or slowing of disease progression will invariably be appreciated, travel requirements and expense, and other hurdles may make the prospect of biweekly treatments for many future years appear burdensome. We can anticipate that some number of families will ask to be "repatriated" to a facility nearer their home town.

We can anticipate that some number of families will ask to be "repatriated" to a facility nearer their home town.

Parents will need information and training in caring for the child between treatments, including assuring the safety of the port. Guidance may address appropriate activities for patients and tactics for mitigating risks of physical activities.

The Company's Role

We can support patients and providers by continuing to collect and share clinical data and potentially arranging meetings in which providers can discuss and develop a set of best practices.

Our IAMs need to be engaged with the institutions regularly to ensure that reimbursement and logistical plans are working smoothly.

Institutional Access Companion Guide

Institution Name: _____

What specific structures and features make this institution ideal to adopt the Product?

Who have you identified as your institutional physician advocate?

Why does this physician have interest in treating CLN2 patients?

Describe this physician's motivation to bring the Product into his/her institution?

How can this advocate connect you to other necessary decision making parties within the institution?

Who are the members of the P&T Committee that will be involved in the review of the Product?

Has a clinical pharmacist been identified to conduct an assessment of the Product? If so who?

What steps will you take with the clinical pharmacist and other members of the P&T Committee to ensure they understand the Product's clinical value proposition?

What Company resources do you plan to use to support the analysis team in their review of the Product?

Who is responsible for conducting the business case for the Product in this institution?

What is the institution's mission statement?

How does the Product support the institution in executing its mission statement?

What experience does this institution have with CLN2 and intraventricular drug administration?

What resources will you use to uncover this key information from your account?

What resources will you share with this institution around reimbursement support?

What resources has the institution already identified to assist with the gap in coverage?

What processes have your institutions used when adopting novel treatments?

Institutional Roles, Responsibilities, and Accountabilities

Who will be responsible for the assessment, treatment and reimbursement of the Product within this institution?

DEPARTMENT	STAKEHOLDER
PHYSICIANS	
select:	
select:	
select:	
select:	
select:	
select:	
select:	
NON-PHYSICIAN PROVIDERS	
select:	
select:	
select:	
select:	
select:	
select:	
select:	
select:	
select:	
select:	
ADMINISTRATIVE	
select:	
select:	
select:	
select:	
select:	
select:	
select:	
OPERATIONAL/TECHNICAL	
select:	
select:	
select:	
select:	
select:	

Institutional Roles, Responsibilities, and Accountabilities

When do these stakeholders and departments collaborate? How can you create an opportunity to unify the decision makers?

What is your strategy to build strong connections with your Company counterparts to ensure effective account management within your institution?

Which member of the patient care team is responsible for developing the treatment plan for the Product?

Once your institution has decided to use the Product, how will you initiate patient onboarding, treatment planning, and logistics planning?

Has this institution identified a location where the Product can be administered and monitored for at least 4.5 hours? Where is this location within the institution?

What is your institution's materials management process for handling special products of this nature? Who is responsible for establishing this process?

Does this institution have freezer space available in a freezer capable of storing the Product at -25 to -15 centigrade?

What EHR system does this institution use, and who is the stakeholder responsible for managing the system?

Intiating the First Treatment

What stakeholders will you invite to the kickoff meeting for the Product?

How will you lead the conversation to ensure the team has the information and support they need to create their treatment plan?

Has this account established guidelines on how to bill for this type of procedure? Who will be responsible for coding these claims at the institution?

What examples can you provide to demonstrate the Company's dedication to the support and education of families and patients?

Who are the key stakeholders who make up the patient care team within this institution? What is their experience in treating CLN2 patients?

What educational materials will you use with the patient care team to ensure they are properly informed for their conversations with patients and their families?

After your institution has successfully delivered its first treatment, what actions will you take to maintain a relationship with your key stakeholders?

Case Study: The Product

Interview with the Chief Pharmacy Officer of the Neurology Center of Excellence

In reviewing novel treatment options like the Product, we would use the processes and approval infrastructure already in place within our institution. In this case, our Pharmacy and Therapeutics (P&T) and Medical Executive Committees would review the Product. This review begins with a physician completing our online formulary request process, which consists of a questionnaire about the Product and its indications.

The review continues with an evaluation assigned to a clinical pharmacist, who collects available information about the Product and data to support its claims. We often request input from other institutions that have the Product, especially rare or novel products, to help inform our evaluation. A subcommittee of specialists in the treatment area—in this case, pediatrics—then reviews the collected product information. For a product like the Product, the subcommittee would include pediatric neurologists, neurosurgeons, nurses, pediatric clinical pharmacists, finance representatives, and possibly an Ethics Committee member. The pharmacy department leads the discussion to determine whether to recommend the Product to the full P&T Committee.

If the subcommittee decides that we would want to use the Product in our institution, we then review the Product with the full P&T Committee. At this point, the discussion is informational: the focus is on the drug's indication, the disease state, pharmacoeconomics, and other factors. The P&T Committee usually accepts the subcommittee's recommendations, but not always. If the P&T Committee accepts the Product, it goes to the Medical Executive Committee for final approval.

That's the typical product approval process, but there are other routes. One example of an alternative route would be going through the Ethics Committee for approval. This Ethics Committee may decide to offer the Product by absorbing its cost through a foundation or other charitable care organization or by offering the Product through self-pay. Another alternative would be evaluating the Product through a clinical trials framework. In this scenario, the Institutional Review Board would establish guidelines and protocols for using the Product in alignment with the primary investigator.

After a product like the Product is approved, we would begin logistics and planning to ensure that we have appropriate processes in place for successful administration without product waste. The team responsible for logistics, scheduling, and procurement varies, but would probably include the pharmacy director, a business manager, a coder, and representatives from manufacturer relations, supply chain, and the clinical care team. The pharmacy director, business manager, coder, and manufacturer relations representative will meet to build a business plan for the Product, including creating a charge description master (CDM) and entering the Product in the

billing system, depending on the outcomes of Ethics Committee discussions. The supply chain department will establish accommodations for procuring the Product.

For products like the Product, we have a special handling process with a signature chain from the delivery driver to the final storage area. When we order volatile or expensive products, we alert the heads of the departments involved in each step in the process so everyone on the team knows to expect the shipment. Even with these precautions, there are occasional breakdowns in the process. For example, a $10,000 product was recently left at the front door of the loading dock, despite explicit instructions for the FedEx driver to get a signature for the delivery. As it turns out, a new driver was filling in while our regular FedEx delivery driver was on vacation and had not been given clear instructions.

Patient scheduling depends on the location of infusion and the location's established processes. Our system has 4 separate infusion suites: oncology, rheumatology, neurology, and gastrointestinal (GI). In our GI infusion suite, a head nurse is responsible for scheduling every patient in the suite. This planning ensures that each patient has been evaluated, we've received prior authorization from each patient's insurance provider, and we've received approval for payment. In contrast, in our oncology infusion suite, an infusion suite coordinator works with a consolidated team to manage the patient load.

After a patient is scheduled, a couple of final logistics come into play before the patient receives the treatment. One is storage. In this case, the subzero freezer may not be near the infusion suite, so transportation must be planned. The pharmacy department generates the prescription and ensures that the Product is handled in compliance with 797 guidelines. The infusion suite's nursing staff manage the equipment and work with materials management to make sure they have all the supplies needed for the infusion. The Product is typically infused with smart pump technology, which the pharmacy department programs.

The most important role you can play in helping an institution with its first participant is supporting education for the team. This would be a big deal to an institution like ours, especially if staff are unfamiliar with intracerebroventricular administration, or intraventricular. The team will want insurance information for creating CDMs. The clinical team will focus on administration procedures, side effect profiles, toxicities, and nuances of the drug. The clinical team will also want to know what to look for when monitoring patients to ensure patient safety. After the Product is approved for use in an institution, you should also provide foundational education for the team to help them establish processes for their first patient, as well as just in time training after the first patient is identified and they are going through the treatment process for the first time.