Monday, December 13, 2021

PAYER

Re: Patient Name

To Whom It May Concern:

I am writing on behalf of my patient, (patient name) who is an (age, sex) to document his/her medical necessity of RYPLAZIM® [plasminogen, human-tvmh] for the treatment of his/her plasminogen deficiency type 1 (hypoplasminogenemia). This letter provides information about the patient’s medical history and diagnosis and a statement summarizing my treatment rationale.

Plasminogen deficiency or hypoplasminogenemia, is a quantitative protein deficiency with decreased plasminogen activity and antigen and is characterized by the accumulation of extravascular fibrin-rich lesions on mucosal surfaces. Individuals with this disease lack a protein called plasminogen, which is responsible for the ability of the body to break down fibrin clots. Plasminogen deficiency is a systemic disorder with lesions that may occur in many organs. Depending on the site and extent of lesions, hypoplasminogenemia may be **life-threatening** or associated with **poor quality of life** or **disability**.

Lesions may develop in many organ systems including the eyes, ears, nose, oral cavity, airways, urinary and genital tracts, gastrointestinal system, skin and central nervous system. Symptoms relate to the extent, size and lesion duration as well as the organ affected. Eye lesions may be associated with photophobia, pain, corneal abrasions and loss of vision; CNS lesions may result in obstructive hydrocephalous, recurrent shunt obstruction, and dandy-walker malformation. Tracheo-bronchial lesions may result in respiratory compromise or obstruction; gingival lesions with resultant loss of bone and dentition; middle ear lesions with hearing impairment or loss; vocal cord lesions with hoarseness or loss of voice; lesions in the female genital tract may cause painful menses and infertility; urinary tract lesions can result in renal obstruction; GI lesions may cause ulcers and what appears to be an inflammatory bowel disease; and wounds may be associated with poor healing. Lesions may develop at any age and may be present for variable time periods. Historically, many treatments have been attempted including surgical removal. Although surgical removal may initially be helpful, it typically results in accelerated lesion regrowth and is not recommended without adequate replacement of the plasminogen level. For further information on this disorder please see the following references *<<include some references, I would include the pivotal trial article as well as one about the disease manifestations itself>>*

Patient’s History and Diagnosis: (Include information here regarding the patient’s condition and specific diagnosis. Also include the patient’s history related to their condition)

|  |  |  |
| --- | --- | --- |
| **Patient’s diagnosis** | **ICD-10** | **Description** |
| ☐ | E88.02 | Plasminogen deficiency |
| ☐ | H10.51 | Ligneous conjunctivitis |
| ☐ | H10.511 | Ligneous conjunctivitis, right eye |
| ☐ | H10.513 | Ligneous conjunctivitis, bilateral |
| ☐ | H10.519 | Ligneous conjunctivitis, unspecific eye |
|  | ***Associated findings*** |
| ☐ | G91.4 | Hydrocephalus |
| ☐ | H67.- | Otitis media |
| ☐ | J99 | Respiratory disorder related to plasminogen deficiency |

Treatment Rationale: The diagnosis of plasminogen deficiency type 1 has been confirmed by:

|  |  |  |  |
| --- | --- | --- | --- |
| **Performed** | **Method** |  | **Value/Gene defect** |
| **☐** | Laboratory  | To determine the plasminogen activity and antigen level |  |
| **☐** | Genetic testing | To confirm suspected Plasminogen Deficiency |  |
| **☐** | Biopsy | To determine if the removed lesion demonstrates a buildup of fibrin-rich deposits when viewed under a microscope |  |

The patient has developed lesions in the following organ systems: organ(s).

*ADD Information, if patient developed eye lesions and they have been surgically removed:*

The lesions in the eye(s) have been removed on Date, as there were no effective treatments available, the lesions returned within xxx weeks/months.

In June 2021 the first and only specific treatment for plasminogen deficiency, a human plasminogen concentrate has been FDA approved. The active ingredient in Ryplazim is plasminogen, purified from human plasma. Treatment with Ryplazim helps to increase the plasma level of plasminogen - enabling a temporary correction of the plasminogen antigen level and reduction or resolution of the lesions. The regimens used in the pivotal study targeted a minimal increased trough activity above baseline levels.

The recommended dosage of RYPLAZIM is 6.6 mg/kg body weight administered intravenously every 2 to 4 days; however, other treatment regimens such as daily infusion may be required based upon the severity of the symptoms or need for intervention. In the pivotal clinical trial, all patients reached the primary endpoint overall rate of clinical success. Overall rate of clinical success is defined as 50% of patients with visible or other measurable non-visible lesions achieving at least 50% improvement in lesion number/size, or functionality impact from baseline. In addition, 78% of all external lesions at baseline and 75% of all internal lesions at baseline were resolved by the end of week 48. No patient developed recurrent or new external or internal lesions.

Duration: RYPLAZIM is temporarily replacing plasminogen in the human body. The therapeutic goal is to increase the trough plasminogen activity by an absolute 10% above baseline. Initial treatment regimens are usually initiated at every three-day intervals; however, individualized needs must be considered as previously stated based upon the site of lesions and clinical status of the patient. The duration of treatment is determined by the health care provider and may be life-long.

Patients who participated in the clinical trial were continued in a compassionate use program and have continued to benefit from the RYPLAZIM treatment. To prevent recurrence of disease manifestations and their associated sequelae, it is required that *<<patient name>>* continue treatment with RYPLAZIM.

Summary: In summary, RYPLAZIM is medically necessary for this patient’s medical condition. Please contact me if any additional information is required to ensure the prompt approval of RYPLAZIM.

Sincerely,

(Physicians name and signature)

Your licensed provider must complete, sign and date the letter