2037: Leukodystrophies Pre-Infusion

The Leukodystrophies Pre-Infusion Data Form is one of the Comprehensive Report Forms. This form captures leukodystrophy specific pre-infusion data such as: disease assessments / laboratory studies at diagnosis, pre-infusion treatment and laboratory studies / clinical status prior to the start of the preparative regimen.

This form must be completed for all recipients whose primary disease is reported on the Pre-TED Disease Classification (2402) Form as a leukodystrophy and specified as one of the following:

- Krabbe Disease (globoid cell leukodystrophy)
- Metachromatic leukodystrophy (MLD)
- Adrenoleukodystrophy (ALD)
- Hereditary diffuse leukoencephalopathy with spheroids (HDLS)

Links to sections of the manual:

- Q1: Subsequent Infusion
- Q2 – 22: Leukodystrophy Diagnosis
- Q23 – 30: Disease Modifying Therapies
- Q31 – 72: Clinical Status Prior to the Preparative Regimen

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please reference the retired manual section on the Retired Forms Manuals webpage.

Date	Manual Section	Add/ Remove/ Modify	Description
7/26/2024	2037: Leukodystrophies Pre-Infusion	Add	Version 2 of the Leukodystrophies Pre-Infusion section of the Forms Instructions Manual released. Version 2 corresponds to revision 4 of the Form 2037.

Q1: Subsequent Transplant or Cellular Therapy

Question 1: Is this the report of a second or subsequent transplant or cellular therapy for the same disease?

Report **No** and go to *Specify the leukodystrophy* question in any of the following scenarios:

- This is the first infusion reported to the CIBMTR; or
- This is a second or subsequent infusion for a different disease (i.e., the patient was previously transplanted for a disease other than a leukodystrophy); or
- This is a second or subsequent infusion for the same disease subtype and this baseline disease insert was not completed for the previous transplant (i.e., the patient was on the TED track for the prior infusion, prior infusion was autologous with no consent, etc.).

Report **Yes** and go to the *Clinical Status Prior to Preparative Regimen* section if this is a subsequent infusion for the same disease and the baseline Leukodystrophies disease form was completed previously.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Q2 – 22: Leukodystrophy Diagnosis

Hereditary diffuse leukoencephalopathy (HDLS)
If the primary disease for infusion is HDLS, manually select this option from *Specify the leukodystrophy subtype*. This option will not auto populate at this time.

Question 2: Specify the leukodystrophy subtype

Indicate the recipient's disease subtype:

- **Krabbe Disease (globoid cell leukodystrophy)**: A rare lysosomal storage disorder affecting the nervous system, most typically occurring in infants.
- **Metachromatic leukodystrophy (MLD)**: A rare genetic disorder in which there is an accumulation of sulfatides, causing damage to the myelin sheath within the nervous system. The three types of MLD are based on age symptoms occur: late-infantile MLD, juvenile MLD, and adult MLD.
- **Adrenoleukodystrophy (ALD)**: A rare genetic disorder causing buildup of very long-chain fatty acids (VLCFAs) and in response, damages the myelin sheath within the nervous system. The most common form of ALD is X-linked ALD, more commonly affecting males.
- **Hereditary diffuse leukoencephalopathy with spheroids (HDLS)**: A rare hereditary disorder affecting adults. The disease is associated with leukoencephalopathy and spheroids in the axons of the brain.

Questions 3 – 4: Specify testing performed to establish the diagnosis (check all that apply)

Specify which testing was performed to establish the diagnosis of the primary disease for infusion, select all that apply.

- **Newborn Screening**: A blood screen which looks for the defective molecules in the circulating blood. In the United States, this blood test is available as part of routine newborn screening. Infants are often diagnosed at birth or in utero.
- **Genetic mutational panel**: A genetic panel is a standard panel of genes known to be associated with hematopoietic abnormalities. The intent of this assessment is to screen for myeloid diseases. This assessment is typically a myeloid mutation panel and is usually labeled as a "Genetic Mutational Panel" within the EMR; however, this varies from institution to institution. If it is unclear if this assessment was performed, seek physician clarification.
- **Laboratory findings (enzyme levels, storage levels, hormone levels)**: Laboratory studies such as enzyme levels, storage levels and hormone levels, may be used to identify deficiencies that cause leukodystrophy.
- **Other Testing**: Includes those methods of testing not already listed above. This option will rarely be used; however, a recipient may be diagnosed as a result of another family member's prior leukodystrophy diagnosis or imaging testing characteristic of the disease. If **Other testing** was performed to establish the diagnosis select this option and specify other testing.

Enzyme / storage activity at diagnosis – recipient

At Diagnosis:
Any testing performed between the date of diagnosis and the start of any treatment for Leukodystrophy.

Questions 5 – 6: Was enzyme / storage activity tested?

Indicate if enzyme / storage activity was tested for the recipient at diagnosis. This type of testing performed is specific to the leukodystrophy subtype. Types of testing include enzyme assays, urine testing, etc. If enzyme / storage activity was tested on the recipient select **Yes** and indicate the date (YYYY-MM-DD) of testing. An example of enzyme activity testing is the quantitative measurement of arylsulfatase A enzyme. If the arylsulfatase A enzyme is deficient, it is the gold standard to confirm a diagnosis of metachromatic Leukodystrophy.

Testing is generally only performed once. In the rare scenario testing is performed multiple times, report the date of the most recent assessment and the results prior to the start of treatment.

If the exact date is not known, use the process described in General Instructions, Guidelines for Completing Forms.

If enzyme / storage activity was not tested for the recipient at diagnosis or it is not known, select **No** or
Unknown, respectively, and continue with *Was the donor / CBU/ a carrier?*

Questions 7 – 8: Recipient result

Indicate whether the results of the recipient's enzyme / storage activity testing were **Normal** or **Abnormal** at diagnosis and if documentation was submitted to CIBMTR (CIBMTR recommends attaching the enzyme / storage activity testing).

For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Enzyme / storage activity at diagnosis – donor

Question 9: Was the donor / CBU a carrier?

Indicate if the donor or CBU was a carrier for a genetic disease / leukodystrophies. If the donor was tested for being a carrier for genetic diseases / leukodystrophies and was negative, select **No** and continue with *Was a genetic mutational panel performed at any time prior to the start of the preparative regimen*. If the donor was not tested, or it is unknown if

testing was performed, select **Unknown** and continue with *Was a genetic mutational panel performed at any time prior to the start of the preparative regimen*.

Questions 10 – 11: Was enzyme activity and / or enzyme substrate tested?

Indicate if enzyme activity and / or enzyme substrate was tested at any time prior to the start of the preparative regimen / infusion. The type of testing performed is specific to leukodystrophy subtype. Types of testing can include enzyme assays, urine testing, etc.

If enzyme / storage activity was tested on the donor select **Yes** and report the date (YYYY-MM-DD) when the donor / CBU was tested. Testing is generally only performed once. In the rare scenario testing is performed multiple times, report the most recent date and results prior to the start of the preparative regimen / infusion.

If the exact date is not known, use the process described in General Instructions, Guidelines for Completing Forms.

If enzyme activity / enzyme substrate was not tested for the donor or it is unknown, select **No** or **Unknown**, respectively and continue with *Was a genetic mutational panel performed at any time prior to the start of the preparative regimen*.

Questions 12 – 13: Donor / CBU testing result

Indicate whether the results of the donor's / CBU's enzyme activity and / or enzyme substrate testing were **Normal** or **Abnormal** and if documentation was submitted to CIBMTR (CIBMTR recommends attaching the enzyme / storage activity testing).

For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Questions 14 – 16: Was a genetic mutational panel performed at any time prior to the start of the preparative regimen? (screening for myeloid diseases)

A genetic panel is a standard panel of genes that are known to be associated with hematopoietic abnormalities. The intent of this assessment is to screen for myeloid diseases and is typically a myeloid mutation panel. This report is usually labeled as a "Genetic Mutational Panel" within the EMR; however, this varies from institution to institution. If it is unclear if this assessment was performed, seek physician clarification.

Indicate **Yes** if a genetic panel was performed at any time prior to the start of the preparative regimen / infusion. If **Yes**, specify if the results of the genetic panel were **Normal** or **Abnormal** and if a copy of the genetic mutation panel was submitted to CIBMTR.

If a genetic panel was not performed or it not known if performed at any time prior to the start of the preparative regimen / infusion, select **No** and continue with *Were the recipient's urinary sulfatides elevated at diagnosis*.

For further instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Question 17: Were the recipient's urinary sulfatides elevated at diagnosis? (MLD recipients only)

Indicate if the recipient's urinary sulfatides were elevated at diagnosis. The analysis of urinary sulfatides is determined through a urine test, often performed for recipients with MLD. If the recipient's urinary sulfatides are elevated above the lab's upper limit of normal (ULN), select **Yes**. If urinary sulfatide analysis was not completed at diagnosis or it is unknown if this analysis was completed, select **No** or **Unknown**, respectively.

Questions 18 – 19: Mean fasting plasma very-long-chain fatty acid (VLCFA) C26:0 level at diagnosis (fasting preferred, but not required) (ALD recipients only)

Indicate if the mean fasting plasma very-long-chain fatty acid (VLCA) level is known at diagnosis, prior to receiving any treatment for ALD. This assessment is typically found within the general lab section of the EMR.

If the mean fasting plasma very-long-chain fatty acid (VLCA) level is **Known**, report the value in µg/mL. If this value is not known, select **Unknown** and continue with *Specify therapy given for adrenal insufficiency with glucocorticoids or mineralocorticoids between diagnosis and infusion*.

Question 20: Specify treatment(s) given for adrenal insufficiency with glucocorticoids or mineralocorticoids between diagnosis and infusion (ALD recipients only) (check all that apply)

Select all treatments given for adrenal insufficiency between diagnosis and the start of the preparative regimen / infusion.

- **Glucocorticoids**: Corticosteroids with anti-inflammatory properties used to treat conditions involving inflammation (e.g., cortisol and cortisone).
- **Mineralocorticoids**: Corticosteroids, assist in regulation of sodium and potassium (e.g., aldosterone).

If the recipient did not receive neither **Glucocorticoids** and / or **Mineralocorticoids** at any time prior to the start of the preparative regimen / infusion, select **None**.

Questions 21 – 22: Specify treatment(s) given to lower plasma very-long-chain fatty acids at any time prior to infusion (check all that apply) (ALD recipients only)

Select all treatments given to lower plasma very-long-chain fatty acids at any time prior to the start of the preparative regimen / infusion.

- **N-acetyl-L-cysteine (NAC)**: (Acetylcysteine) is a supplement of cysteine (amino acid). Cysteine is an antioxidant agent that assists with respiratory conditions, fertility, and brain health.
- **GTE:GTO oil (Lorenzo's oil)**: Composed of erucic acid and oleic acids. Known to decrease / lower very long chain fatty acids (VLCA) levels.
- **Other treatment**: Includes those treatments not already listed above. If the recipient received treatments not listed, such as experimental clinical trials, select this option and specify the other treatment(s). Report the generic name of the agent, not the brand name.

If no therapy was given at any time prior to the start of the preparative regimen / infusion, select **None.**

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Q23 – 29: Disease Modifying Therapies

Question 23: Were disease modifying therapies given? (excludes blood transfusions)

Indicate if the recipient received disease modifying therapies at any time between the diagnosis and the start of the preparative regimen, excluding blood transfusion(s) (review the question below for a list of common disease modifying therapies).

If the recipient did not receive disease modifying therapies or if no information is available to determine if the recipient received disease modifying therapies, select **No** or **Unknown**, and continue with *Was enzyme activity and/or enzyme substrate tested*?

Reporting Multiple Disease Modifying Therapies
FormsNet3℠ application: Complete questions *Specify the disease modifying therapy, Date therapy started, and Date therapy stopped* for each disease modifying therapy administered by adding an additional instance in FormsNet3SM application.
Paper form submission: Copy questions *Specify the disease modifying therapy, Date therapy started, and Date therapy stopped* and complete for each disease modifying therapy administered.

Same Therapy Restarted
If the same therapy was started and stopped multiple times prior to the start of the preparative regimen, only one instance needs to be reported. In this case, report the therapy start date as the date therapy first began.

Questions 24 – 25: Specify the disease modifying therapy (check all that apply)

Select the disease modifying therapy administered as part of the line of therapy being reported.

- **Leriglitazone**: a novel selective peroxisome proliferator-activated receptor gamma agonist.

If the recipient received a therapy which is not listed, select **Other** and specify the treatment. Report the generic name of the agent, not the brand name.

Questions 26 – 27: Date therapy started

Indicate if the therapy start date (YYYY-MM-DD) is known. If **Known**, report the first date the recipient began this line of therapy.

If the exact date is not known report an estimated date and check the **Date estimated** box. Refer to General Instructions, General Guidelines for Completing Forms for information about reporting estimated dates.

Questions 28 – 29: Date therapy stopped

Indicate if the stop date is known. If the therapy stop date is **Known**, report the date (YYYY-MM-DD) when the therapy end. If the therapy is being given in cycles, report the end date as the date when the recipient started the last cycle for this line of therapy. Otherwise, report the final administration date for the therapy being reported.

If the exact date is not known report an estimated date and check the **Date estimated** box. Refer to General Instructions, General Guidelines for Completing Forms for information about reporting estimated dates.

Report **Not applicable** if the recipient is still receiving therapy at the start of the preparative regimen / infusion.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Q30 – 71: Clinical Status Prior to Preparative Regimen

Testing Prior to the Start of the Preparative Regimen / Infusion:
Report all findings within two months prior to the start of the preparative regimen / infusion for the Clinical Status Prior to Preparative Regimen section. If an assessment was performed multiple times, report the most recent results.

Enzyme activity / enzyme substrate testing:
Do not include the recipient's results of enzyme activity / enzyme substrate testing performed at diagnosis.

Questions 30 – 31: Was enzyme activity and/or enzyme substrate tested?

Indicate if the recipient was tested for enzyme activity and / or enzyme substrate prior to the start of the preparative regimen / infusion. The type of testing performed is specific to leukodystrophy subtype. Types of testing can include enzyme assays, urine testing, etc.

If the recipient's enzyme activity and / or enzyme substrate was tested, select **Yes** and report the date (YYYY-MM-DD) of testing. If testing is performed multiple times, report the most recent date and results prior to the start of the preparative regimen / infusion.

If the exact date is not known, use the process described in General Instructions, Guidelines for Completing Forms.

If the enzyme activity and / or enzyme substrate was not tested prior to the start of the preparative regimen / infusion or it is unknown if testing occurred, select **No** or **Unknown**, respectively and continue with *Was the total neurologic function scale (NFS) score obtained*.

Questions 32 – 33: Recipient result

Indicate whether the results of the recipient's enzyme activity and / or enzyme substrate testing were **Normal** or **Abnormal** and if documentation was submitted to CIBMTR (CIBMTR recommends attaching the enzyme / storage activity testing).

For further instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Questions 34 – 35: Was the total neurologic function scale (NFS) score obtained? (ALD recipients only)

The total neurologic function scale (NFS) is a 25-point scale used to assess severity of neurological dysfunction and is done by scoring 15 disabilities.

Indicate **Yes** or **No** if a NFS score was obtained prior to the preparative regimen / infusion. This information will be documented within a physician's note.

If a total NFS score was obtained, select **Yes**, and report the date (YYYY-MM-DD) of assessment. If the total NFS was obtained multiple times prior to the preparative regimen / infusion, report the date and results of the most recent assessment.

If the exact date is not known, use the process described in General Instructions, Guidelines for Completing Forms.

If the total NFS score was not obtained prior to the preparative regimen / infusion or it is not known if a score was obtained, select **No**, and continue with *Is there a history of seizures attributed to the underlying disease at any time prior to the preparative regimen*.

Total Neurologic Function Scale (NFS) Score and Domain Clinical Scores

When reporting the total NFS and domain clinical scores, report the scores based on documentation within the physician's progress note. If the total NFS score is documented but the domain clinical scores are not provided, only report the total NFS score and leave the data fields for the domain clinical scores blank. Similarly, if only the domain clinical scores

Question 36: Specify total neurologic function scale score

Report the total neurologic function scale (NFS) score as documented by the physician. The total NFS score will be a value between 1-25.

If the NFS score is not known and only the domain clinical scores are documented, leave this data field blank.

Questions 37 – 52: Select known domain clinical score(s) (check all that apply)

Select the known domain clinical score(s) and report the score(s) as documented by the physician.

- **Hearing / auditory processing problems**: Trouble with hearing.
- **Aphasia / apraxia**: Speech disorder / impairment.
- **Loss of communication**: Loss of the ability to communicate.
- **Vision impairment / fields cut**: Reduced field of vision.
- **Cortical blindness**: Total or partial loss of vision due to damage to the occipital cortex.
- **Swallowing difficulty or other central nervous system dysfunction**: Dysphagia due to damage of the nervous system.

- **Tube feeding**: Percutaneous endoscopic gastrostomy (PEG), esophagogastroduodenoscopy (EGD), or G-tube insertion.
- **Running difficulties / hyperreflexia**: Muscles are less responsive to stimuli. Causing trouble holding, running, driving etc.
- **Walking difficulties / spasticity / spastic gait (no assistance)**: Trouble walking, and / or abnormal muscle tightness due to prolonged muscle contractions.
- **Spastic gait (needs assistance) wheelchair required**: Stiff, often foot dragging walk, due to prolonged muscle contractions on one side. Assistance with wheelchair required.
- **No voluntary movement**: Absence of voluntary movements such as moving fingers, toes, sitting upright, etc.
- **Episodes or urinary or fecal incontinency**: Loss of bladder and / or bowel control with episodes of any urinary or bowel incontinence.
- **Total urinary or fecal incontinency**: Total loss of bladder and / or bowel control. This will require continuous use of a catheter.
- **Nonfebrile seizures**: A single, uncontrolled electrical activity in the brain, which may produce a physical convulsion, minor physical signs, thought disturbances or a combination of symptoms. Nonfebrile seizures are characterized as spontaneous recurrent seizures unrelated to fever.

If only the total NFS score is known and not the domain clinical scores, leave these questions blank.

Question 53: Is there a history of seizures attributed to the underlying disease at any time prior to the preparative regimen?

Indicate **Yes** if there was a history of seizures attributed to the underlying disease at any time prior to the preparative regimen / infusion. If there was no history of seizures attributed to the underlying disease or it is not known, indicate **No**, and continue with *Was cerebrospinal fluid (CSF) testing done prior to the preparative regimen*.

Question 54: Were any of the seizures considered nonfebrile?

Report **Yes** if any of the seizures prior to the preparative regimen / infusion were considered nonfebrile (spontaneous recurrent seizures unrelated to fever). If all seizures prior to the start of the preparative regimen / infusion were febrile, select **No**.

Questions 55 – 56: Was cerebrospinal fluid (CSF) testing done prior to the preparative regimen?

Indicate if cerebrospinal fluid (CSF) testing was completed prior to the preparative regimen / infusion. CSF is collected via lumbar puncture or spinal tab.

If testing was performed, select **Yes** and report the date (YYYY-MM-DD) of the most recent CSF testing.

If the exact date is not known, use the process described in General Instructions, Guidelines for Completing Forms.

If CSF testing was not performed prior to the preparative regimen / infusion or it is not known, select **No** or **Unknown**, respectively and continue with *Date of most recent magnetic resonance imaging (MRI) prior to the preparative regimen*.

Questions 57 – 59: Specify known CSF result(s) (check all that apply)

Report the known CSF results.

- **Opening Pressure**: Opening pressure is measured during the lumbar puncture; this is a measurement of intracranial pressure. If the opening pressure is known, select this option and report the opening pressure value.

- **Total Protein**: Total protein is a measurement used to determine the levels of protein in cerebrospinal fluid. If the total protein is known, select this option and report the CSF total protein value.

In the rare case where neither the opening pressure or the total protein was known, leave *Specify known CSF result(s)* blank, override the validation error using the code "unknown," and continue with *Date of most recent magnetic resonance imaging (MRI) prior to the preparative regimen*.

Question 60: Date of most recent MRI prior to the preparative regimen

Magnetic resonance imaging (MRI) is an imaging technique used to form pictures of the anatomy and the physiological processes of the body. MRIs are used to assess recipient's with leukodystrophy.

Report the date (YYYY-MM-DD) of the most recent MRI performed prior to the preparative regimen / infusion.

If the exact date is not known, use the process described in General Instructions, Guidelines for Completing Forms.

Question 61: Specify MRI results

Specify the results of the most recent MRI performed prior to the start of the preparative regimen / infusion. Indicate if the results were **Normal** or **Abnormal** as determined by the radiologist or physician.

Questions 62 – 64: Was gadolinium contrast used for this assessment?

Gadolinium contrast is often used in MRI assessments to enhance imagining, improving the visibility of inflammation, blood vessels and blood supply.

If gadolinium contrast was used, select **Yes** and indicate if gadolinium enhancement was reported. If gadolinium contrast was used, gadolinium enhancement will be noted in the MRI report and can be suggestive of abnormalities. Additionally, specify if a copy of the MRI report is attached in FormsNet3^{SM} (CIBMTR recommends attaching the MRI report).

If gadolinium contrast was not used in the MRI assessment, select **No** and continue with *Was documentation submitted to the CIBMTR*.

For instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Questions 65-66: Were nerve conduction velocities tested at any time prior to the preparative regimen?

Nerve conduction velocity (NCV) testing measures how quickly an electrical impulse moves through the nerve and can identify nerve damage. This procedure is typically performed by a neurologist.

Indicate if NCV testing was performed at any time prior to the preparative regimen / infusion. If **Yes**, report the date (YYYY-MM-DD) of the most recent testing. If NCV testing was not done or it is unknown, report **No** or **Unknown**, respectively and continue with *Was a neurocognitive test administered at any time prior to the preparative regimen*.

Questions 67-68: Specify Results

Report whether the results of the recipient's NCV testing were **Normal** or **Abnormal**. Additionally, indicate if documentation was submitted to CIBMTR (CIBMTR recommends attaching the nerve conduction velocities tests).

The results of the NCV test may be found in the procedure / results report or in the neurologist's note. For instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 69-71: Was a neurocognitive test administered at any time prior to the preparative regimen?

A neurocognitive test is an assessment completed by a neuropsychologist, used to assess the cognitive function of a recipient. Indicate if a neurocognitive test was administered at any time prior to the preparative regimen / infusion. This information will be found within a progress note by the neuropsychologist.

If neurocognitive testing was performed, indicate **Yes**, and report the date (YYYY-MM-DD) of the most recent assessment. Specify if documentation of mental development neurocognitive testing was submitted to the CIBMTR. It is highly encouraged to attach this assessment / documentation. Additionally, complete the Neurocognitive Assessment (3503) Form.

If testing was not done or it is unknown, indicate **No** or **Unknown**, respectively and continue to the signature line.

For instructions on how to attach documents in FormsNet3SM, refer to the Training Guide.

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Q72: Marrow Evaluation

Marrow evaluation

This section is only completed for gene therapy infusions.

Question 72: Was a marrow aspirate and / or biopsy performed?

Indicate **Yes** or **No** if a marrow aspirate and or biopsy was performed in this reporting period. If **Yes**, complete the Laboratory Studies (3502) Form and Marrow Surveillance (3506) Form. The intent is to screen for and/or identify changes in the marrow such as dysplasia, MDS, or new hematologic malignancy

Report **Unknown** if not documented.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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