azurity pharmaceuticals

Xatmep®
(methotrexate)
Oral Solution
2.5 mg/mL

SAMPLE LETTER OF MEDICAL NECESSITY

This sample letter beginning on page two and related information is provided for informational purposes only.

It provides an example of the types of information that may be provided when responding to a request from a patient's health plan/insurer to provide a letter of medical necessity for Xatmep® (methotrexate) Oral Solution.

Health plan requirements may vary, so the prescriber should refer to the prior authorization or coverage information specific to their patient's health plan before completing a Letter of Medical Necessity.

Use of the information in this letter does not guarantee coverage or that the health plan will provide reimbursement for Xatmep® (methotrexate) and is not intended to be a substitute for or to influence the independent medical judgment of the physician.

It is the responsibility of the prescriber and/or their office staff, as appropriate, to determine the correct diagnosis, treatment protocol, and content of all such letters and related forms for each individual patient.

The prescriber should refer to the Important Safety Information in the full Prescribing Information when determining whether the product is medically appropriate for a patient.

SAMPLE LETTER OF MEDICAL NECESSITY

Patient:_____
PATIENT NAME

Group/Policy Number:_____ Date(s) of service:_____
GROUP / POLICY NUMBER *DATE(S) OF SERVICE*

Diagnosis:_____
DIAGNOSIS CODE AND DESCRIPTION

Dear_____:
CONTACT NAME OR DEPARTMENT

I am writing on behalf of my patient,_____
PATIENT NAME

to_____
REQUEST PRIOR AUTHORZATION/DOCUMENT MEDICAL NECESSITY

for treatment with Xatmep® (methotrexate) Oral Solution. Xatmep® (methotrexate) is indicated for treatment of _____

_____This letter serves to document
INDICATION STATEMENT

that _____has a diagnosis of
PATIENT NAME

_____
DIAGNOSIS / CODE

and needs treatment with Xatmep® (methotrexate) Oral Solution, and that Xatmep® (methotrexate) is medically necessary for

_____as prescribed. On behalf of_____,
HIM/HER *PATIENT NAME*

I am requesting approval for use and subsequent payment for the treatment with Xatmep® (methotrexate).

SUMMARY OF PATIENT MEDICAL HISTORY AND DIAGNOSIS

_____ is a _____-year-old _____.
PATIENT NAME *AGE* *MALE/FEMALE*

Diagnosed with_____.
DIAGNOSIS

_____has been in my care since _____.
PATIENT NAME *DATE*

As a result of_____,
DIAGNOSIS

my patient_____.
ENTER BRIEF DESCRIPTION OF PATIENT HISTORY AND RECENT PRESENTATION

In my professional opinion, _____'s likely prognosis without treatment with
PATIENT NAME

Xatmep® (methotrexate),_____.
PROVIDE SUMMARY OF MEDICAL OPINION

CLINICAL RATIONALE FOR XATMEP® (METHOTREXATE) ORAL SOLUTION

Given_____'s medical history, condition, and the supporting clinical
PATIENT NAME

information _____,
ATTACHED SUPPORTING MEDICAL RECORDS, LABORATORY REPORTS, ETC.

I believe treatment of_____ with_____ is warranted,
PATIENT NAME *PRODUCT*

appropriate and medically necessary. Xatmep® (methotrexate) is indicated for_____.
DRUG INDICATION

The accompanying prescribing information provides the approved clinical information for Xatmep® (methotrexate).

The plan of treatment is to start the patient on Xatmep® (methotrexate),_____.
PROVIDE TREATMENT COURSE

In summary, Xatmep® (methotrexate) is medically necessary and reasonable for_____'s
PATIENT NAME

medical condition and warrants coverage. Please contact me at_____if you require additional
PHYSICIAN TELEPHONE NUMBER

information about this case. Thank you for your prompt attention.

Sincerely,

_____, _____
PHYSICIAN NAME *PHYSICIAN DEGREE*

IMPORTANT SAFETY INFORMATION

XATMEP® (methotrexate) Oral Solution, 2.5 mg/mL

WARNING: SEVERE TOXIC REACTIONS, INCLUDING EMBRYO-FETAL TOXICITY

See Full Prescribing Information for complete boxed warning.

Methotrexate can cause the following severe or fatal adverse reactions.

Monitor closely and modify dose or discontinue methotrexate as appropriate.

- Bone marrow suppression (5.1)
- Serious infections (5.2)
- Renal toxicity and increased toxicity with renal impairment (5.3)
- Gastrointestinal toxicity (5.4)
- Hepatic toxicity (5.5)
- Pulmonary toxicity (5.6)
- Hypersensitivity and dermatologic reactions (5.7)
- Methotrexate can cause embryo-fetal toxicity, including fetal death. Use in pJIA is contraindicated in pregnancy. Consider the benefits and risks of XATMEP and risks to the fetus when prescribing XATMEP to a pregnant patient with a neoplastic disease. Advise females and males of reproductive potential to use effective contraception during and after treatment with XATMEP (4, 5.9, 8.1, and 8.3).

INDICATIONS:

XATMEP is a folate analog metabolic inhibitor indicated for the:

- Treatment of pediatric patients with acute lymphoblastic leukemia (ALL) as part of a multi-phase, combination chemotherapy maintenance regimen.
- Management of pediatric patients with active polyarticular juvenile idiopathic arthritis (pJIA) who have had an insufficient therapeutic response to, or are intolerant of, an adequate trial of first-line therapy including full dose non-steroidal anti-inflammatory agents (NSAIDs).

ADDITIONAL IMPORTANT SAFETY INFORMATION:

Contraindications:

XATMEP is contraindicated in pregnant patients with non-malignant disease and in patients with severe hypersensitivity to methotrexate.

Warnings and Precautions:

XATMEP suppresses hematopoiesis and can cause severe and life-threatening pancytopenia, anemia, leukopenia, neutropenia, and thrombocytopenia. Obtain blood counts at baseline and periodically; monitor patients for complications of bone marrow suppression.

Patients treated with XATMEP are at increased risk for developing life-threatening or fatal bacterial, fungal, or viral infections, including Pneumocystis jiroveci pneumonia, invasive fungal infections, hepatitis B reactivation, tuberculosis (primary or reactivation), disseminated Herpes zoster and cytomegalovirus infections.

XATMEP can cause renal damage, including acute renal failure. Monitor renal function. Consider administration of glucarpidase in patients with toxic plasma methotrexate concentrations (> 1 micromole/liter) and delayed clearance due to impaired renal function.

XATMEP can cause diarrhea, stomatitis, vomiting, hemorrhagic enteritis, and fatal intestinal perforation. Patients with peptic ulcer disease and ulcerative colitis are at increased risk for severe gastrointestinal adverse reactions. Unexpected severe and fatal gastrointestinal toxicity can occur with concomitant use of NSAIDs.

Hepatic toxicity: severe and potentially irreversible hepatotoxicity, including fibrosis, cirrhosis, and fatal liver failure can occur. Avoid use of XATMEP in patients with chronic liver disease.

Pulmonary toxicity: acute or chronic interstitial pneumonitis and irreversible or fatal cases can occur at all dose levels.

Hypersensitivity: Severe, including fatal, dermatologic reactions such as toxic epidermal necrolysis, Stevens-Johnson syndrome, exfoliative dermatitis, skin necrosis, erythema multiforme can occur. Anaphylaxis or other serious hypersensitivity reactions can occur. Discontinue methotrexate and institute appropriate therapy. Radiation dermatitis and sunburn may be "recalled."

Secondary malignancies can occur at all dose levels. Lymphoproliferative disease has been reported with low-dose oral methotrexate which regressed when methotrexate was withdrawn.

Methotrexate can cause embryo-fetal toxicity and fetal death when administered during pregnancy. In pregnant women with non-malignant disease, methotrexate is contraindicated. Consider the risks and benefits of XATMEP and risks to the fetus when prescribing to a pregnant patient with a neoplastic disease. Advise females of reproductive potential to use effective contraception during therapy and for 6 months after the final dose. Advise males of reproductive potential to use effective contraception during and for at least 3 months after the final dose.

Immunizations may be ineffective when given during XATMEP therapy.

Immunization with live virus vaccines is not recommended during XATMEP therapy.

Effects on reproduction: Methotrexate can cause impairment of fertility, oligospermia, and menstrual dysfunction. It is unknown if the infertility is reversible in affected patients.

Increased toxicity due to third-space accumulation can occur. Evacuate significant third-space accumulation prior to methotrexate administration

Concomitant radiation therapy increases the risk of soft tissue necrosis and osteonecrosis associated with methotrexate.

Closely monitor laboratory parameters for hematology, renal function, and liver function. Increase monitoring during initial dosing, dose changes, and during periods of increased risk of elevated methotrexate blood levels (e.g., dehydration).

Pulmonary function tests may be useful if methotrexate-induced lung disease is suspected, especially if baseline measurements are available.

Risk of improper dosing: Once-weekly dosing is appropriate. Fatal toxicity has been reported with daily dosing. An accurate milliliter measuring device should be used. Inform patients that a household teaspoon is not an accurate measuring device and could lead to overdosage.

Adverse Reactions: *See Full Prescribing Information for additional Adverse Reactions (6).*

Most common adverse reactions are ulcerative stomatitis, leukopenia, nausea, and abdominal distress.

Other frequently reported reactions are malaise, fatigue, chills and fever, dizziness, and decreased resistance to infection.

The approximate incidences of adverse reactions reported in pediatric patients with JIA treated with oral, weekly doses of methotrexate (5 to 20 mg/m^2/week or 0.1 to 0.65 mg/kg/week) were as follows (virtually all patients were receiving concomitant non-steroidal anti-inflammatory drugs, and some also were taking low doses of corticosteroids): elevated liver function tests, 14%; gastrointestinal reactions (e.g., nausea, vomiting, diarrhea), 11%; stomatitis, 2%; leukopenia, 2%; headache, 1.2%; alopecia, 0.5%; dizziness, 0.2%; and rash, 0.2%. Although there is experience with dosing up to 30 mg/m^2/week in JIA, the published data for doses above 20 mg/m^2/week are too limited to provide reliable estimates of adverse reaction rates.

Drug Interactions:

Penicillins may reduce the clearance of methotrexate; increased serum concentrations of methotrexate with concomitant hematologic and gastrointestinal toxicity have been observed with methotrexate. Monitor patients accordingly.

Trimethoprim/sulfamethoxazole has been reported to increase bone marrow suppression in patients receiving methotrexate. Monitor patients accordingly.

Hepatotoxins: May increase hepatotoxicity. Monitor patients receiving concomitant hepatotoxins for signs of hepatotoxicity.

Probenecid may reduce renal elimination of methotrexate; consider alternative drugs.

Nitrous oxide as an anesthetic potentiates the effect of methotrexate resulting in the potential for increased toxicity.

NSAIDs, Aspirin, and Steroids: Concomitant administration of some NSAIDS with high dose methotrexate therapy has been reported to elevate and prolong serum methotrexate levels, resulting in deaths from severe hematologic and gastrointestinal toxicity.

Methotrexate may decrease theophylline clearance. Monitor theophylline levels.

Use in Specific Populations:

See Full Prescribing Information for Additional Information (8).

Pregnancy

Methotrexate can cause embryo-fetal toxicity and fetal death when administered to a pregnant woman.

Lactation

Advise women not to breastfeed during XATMEP therapy.

Inform caregivers and patients of the need for proper storage and disposal of dispensing bottles and dosing devices. Keep this and all medications out of reach of children.

This Important Safety Information does not include all the information needed to use XATMEP safely and effectively. Visit XATMEP.com for Full Prescribing Information.

To report SUSPECTED ADVERSE REACTIONS, contact Azurity Pharmaceuticals, Inc. at 1-800-461-7449, or FDA at 1-800-FDA-1088 or www.fda.gov/MedWatch.

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