GOLD COAST HEALTH PLAN TOTAL Care ADVANTAGE℠

TOTAL CARE ADVANTAGE PART B CLINICAL GUIDELINES

TYSABRI *(natalizumab),* injection for IV use
TYRUKO *(natalizumab-sztn),* injection for IV use (biosimilar)

<table>
<tr><th>PA Criteria</th><th>Criteria Details</th></tr>
<tr><td>Description</td><td>Natalizumab (Tysabri®) and its biosimilar, natalizumab-sztn (Tyruko®), are integrin receptor antagonists.</td></tr>
<tr><td>Covered Uses
(FDA approved indication)</td><td>TYSABRI and TYRUKO are indicated for the treatment of:
a. Multiple Sclerosis (MS) – indicated as monotherapy for the treatment of relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.
b. Crohn’s Disease (CD) – indicated for inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn’s disease with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of TNF-α. In CD, TYSABRI should NOT be used in combination with immunosuppressants or inhibitors of TNF-α.</td></tr>
<tr><td>Dosing and Administration</td><td>
<table>
<tr><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td>Multiple Sclerosis;
Crohn’s Disease</td><td>300 mg IV infusion Q4 weeks
<table>
<tr><th></th><th>Infusion Time</th><th>Post-Infusion Observation</th></tr>
<tr><td>1st 12 infusions</td><td>60 min</td><td>60 min</td></tr>
<tr><td>13th infusion and on</td><td>60 min</td><td>PRN</td></tr>
</table>
DO NOT administer as IV push or bolus</td><td>300 mg</td></tr>
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</td></tr>
<tr><td>Billing and Coding Information</td><td>
<table>
<tr><th></th><th>10-digit NDC</th><th>11-digit NDC</th></tr>
<tr><td>TYSABRI</td><td>64406-008-01</td><td>64406-0008-01</td></tr>
<tr><td>TYRUKO</td><td>61314-543-94</td><td>61314-0543-94</td></tr>
</table>
<table>
<tr><th>HCPCS Code</th><th>Description</th></tr>
<tr><td>J2323</td><td>Injection, natalizumab, 1 mg (TYSABRI)</td></tr>
<tr><td>Q5134</td><td>Injection, natalizumab-sztn, biosimilar, 1 mg (TYRUKO)</td></tr>
</table>
<table>
<tr><th>CPT Procedural Codes</th><th>Description</th></tr>
<tr><td>96365</td><td>IV infusion, up to one hour</td></tr>
<tr><td>96413</td><td>Chemotherapy IV infusion, up to one hour</td></tr>
</table>
</td></tr>
<tr><td>Product Availability</td><td>Single-dose vial: 300 mg/15 mL (20 mg/mL) solution for dilution</td></tr>
<tr><td>Contraindications</td><td>Patients who have or have had Progressive Multifocal Leukoencephalopathy (PML); patients who have had a hypersensitivity reaction to TYSABRI.</td></tr>
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GOLD COAST HEALTH PLAN
TOTAL Care ADVANTAGE℠

Recommended Medical Monitoring	**BLACK BOX WARNING: Progressive Multifocal Leukoencephalopathy (PML)** – Natalizumab products increase the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability. A. Risk factors for the development of PML include the presence of antiJCV antibodies, duration of therapy, and prior use of immunosuppressants. These factors should be considered in the context of expected benefit when initiating and continuing treatment with Natalizumab. B. Monitor patients, and withhold therapy immediately at the first sign or symptom suggestive of PML. C. Because of the risk of PML, TYSABRI and TYRUKO are available only through **REMS**. Natalizumab is also associated with: A. Herpes infections B. Hepatotoicity C. Hypersensitivity reactions, including anaphylaxis D. Immunosuppression/infections E. Hematological abnormalities, including thrombocytopenia
Approval Criteria **Multiple Sclerosis**	A. Physician administered IV infusion; in-office or HOPD i. Cannot be self-administered B. Multiple Sclerosis **(must meet all)**: i. Diagnosis of relapsing forms of MS, including clinically isolated syndrome, relapsing-remitting disease and active secondary progressive disease ii. Prescribed by or in consultation with a neurologist iii. Age ≥ 18 years iv. TYSABRI and TYRUKO are not prescribed concurrently with other disease modifying therapies for MS (see Appendix) v. Dose does not exceed 300 mg (one vial) every four weeks
Crohn's Disease	C. Crohn's Disease **(must meet all)**: i. Diagnosis of Crohn's Disease ii. Prescribed by or in consultation with a gastroenterologist iii. Age ≥ 18 years iv. Member meets one of the following: 1. Failure of a ≥ three consecutive month trial of at least ONE immunomodulator (e.g., azathioprine, 6-mercaptopurine [6-MP], methotrexate [MTX]) at up to maximally indicated doses, unless contraindicated, clinically significant adverse effects are experienced, or previously failed a biologic agent for CD 2. Medical justification supports inability to use immunomodulators v. Member meets one of the following, unless clinically significant adverse effects are experienced or all are contraindicated: 1. Failure of one* adalimumab product (e.g., Hadlima™, Simlandi®, Yusimry™, adalimumab-aaty, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred), used for ≥ three consecutive months 2. History of failure of two TNF blockers

GOLD COAST HEALTH PLAN
TOTAL Care ADVANTAGE℠

	vi. Failure of a ≥ three consecutive month trial of one ustekinumab product (e.g., Otulfi®, Pyzchiva®, Selarsdi™, Steqeyma®, Yesintek), unless clinically significant adverse effects are experienced or all are contraindicated vii. Tysabri and Tyruko are not prescribed concurrently with immunosuppressants (e.g., azathioprine, cyclosporine, 6-MP, MTX) or TNF-α inhibitors (note: aminosalicylates may be continued. viii. Dose does not exceed 300 mg (one vial) every four weeks.
Age Restriction	Adults ≥ 18 years old
Coverage Duration	**Initial:** six months. **Reauthorization:** 12 months. Dose will be approved according to the FDA approved labeling or within accepted standards of medical practice.
Other Criteria (LCD, NCD, etc.)	None.
Misc Info, Appendix Etc.	**Therapeutic Alternatives for Multiple Sclerosis** a. Aubagio (teriflunomide) b. Avonex, Rebif (interferon beta-1a) c. Betaseron, Extavia (interferon beta-1b) d. Copaxone, Glatopa (glatiramer acetate) e. Gilenya (fingolimod) f. Plegridy (peginterferon beta-1a) g. Tecfidera (dimethyl fumarate) **Therapeutic Alternatives for Crohn's Disease** a. Avsola, Renflexis, Inflectra (infliximab) b. Azasan, Imuran (azathioprine) c. Cimzia (certolizumab) d. Corticosteroids e. Hadlima, Simlandi, Yusimry, Yuflyma, Hyrimoz, Hulio, Cyltezo (adalimumab's) f. Otulfi, Pyzchiva, Selarsdi, Steqeyma, Yesintek (ustekinumab's) g. Pentasa (mesalamine) h. Prograf (tacrolimus) i. Purixan (6-mercaptopurine) j. Rasuvo, Otrexup (methotrexate)

STATUS	DATE REVISED	REVIEW DATE	APPROVED/REVIEWED BY	EFFECTIVE DATE
Created	1/14/26	1/14/26	Tamara Chinarian, PharmD, Clinical Pharmacist	N/A
Approved	N/A	2/12/26	Pharmacy & Therapeutics (P&T) Committee	2/12/26