Clinical Policy: Triptans

Reference Number: CP.CPA.217
Effective Date: 11.16.16
Last Review Date: 11.24
Line of Business: Commercial

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

The following are triptans requiring prior authorization and/or quantity limits: almotriptan, eletriptan (Relpax®), frovatriptan (Frova®), naratriptan, sumatriptan (Imitrex®), sumatriptan injection (Imitrex, Zembrace™ SymTouch™), sumatriptan nasal powder (Onzetra™ Xsail™), sumatriptan nasal spray (Imitrex, Tosymra™), sumatriptan/naproxen (Treximet®), rizatriptan (Maxalt®, Maxalt-MLT®, RizaFilm®), zolmitriptan (Zomig®, Zomig® ZMT) and zolmitriptan nasal spray (Zomig).

FDA Approved Indication(s)

Triptans are indicated for the acute treatment of migraine attacks with or without aura in:

- Adults (all products)
- Pediatric patients (certain products only):
  - Almotriptan: age 12 to 17 years with a history of migraine attacks usually lasting 4 hours or more (when untreated)
  - Maxalt, Maxalt MLT: age 6 to 17 years old
  - RizaFilm: age 12 to 17 years of age weighing 40 kg or more
  - Treximet, Zomig Nasal Spray: age 12 to 17 years

Imitrex injection is additionally indicated for the acute treatment of cluster headache in adults.

Limitation(s) of use:

- Use only if a clear diagnosis of migraine has been established. If a patient has no response to the first migraine attack treated with a specific triptan, reconsider the diagnosis of migraine before that triptan is administered to treat any subsequent attacks.
- Triptans are not indicated for the prevention of migraine attacks.
- All triptans except Imitrex injection: safety and effectiveness of triptans have not been established for cluster headache.
- Imitrex injection: not indicated for the preventative treatment of cluster headache attacks.
- In adolescents age 12 to 17 years, efficacy of almotriptan on migraine-associated symptom (nausea, photophobia, and phonophobia) was not established.
- Almotriptan and Maxalt are not intended for use in the management of hemiplegic or basilar migraine.
- Zomig Nasal Spray is not recommended in patients with moderate to severe hepatic impairment.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that almotriptan, Frova, Imitrex, Imitrex injection, Maxalt, Maxalt MLT, naratriptan, Onzetra Xsail, Relpax, RizaFilm, Tosymra, Treximet, Zembrace SymTouch, Zomig, and Zomig ZMT are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Migraines – Oral Agents (*see Sections I.B and I.C for non-oral triptans*) (must meet all)**:**

1. Diagnosis of migraine headaches;
2. Request is for an oral agent;
3. Member meets the following age requirements (a, b, or c):
   a. For naratriptan, Frova, Imitrex, Relpax, Zomig, Zomig-ZMT: Age ≥ 18 years;
   b. For almotriptan, RizaFilm, Treximet: Age ≥ 12 years;
   c. For Maxalt, Maxalt-MLT: Age ≥ 6 years;
4. For non-preferred agents (including Frova, Relpax, Treximet, Zomig, Zomig-ZMT), member meets one of the following (a or b):
   a. Failure of at least TWO formulary generic $5HT_1$-agonist migraine medications (e.g., almotriptan, naratriptan, rizatriptan/rizatriptan ODT, sumatriptan succinate) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;
   b. For Treximet requests for members age 12 – 17 years: Failure of almotriptan and rizatriptan, unless clinically significant adverse effects are experienced or both are contraindicated;
5. For RizaFilm requests: Member weighs ≥ 40 kg;
6. For all Treximet requests: Medical justification supports inability to use the individual components (i.e., sumatriptan and naproxen) concurrently (e.g., contraindications to the excipients of all brand and generic products);
7. For requests of monthly quantities greater than the health plan limit but ≤ 2 times the health plan limit, member meets **one** of the following (a or b):
   a. Failure of TWO prophylactic migraine medications, unless clinically significant adverse effects are experienced or all are contraindicated *(see Appendix B)*;
   b. Member is being treated by or in consultation with a neurologist, headache, or pain specialist;
8. For requests of monthly quantities > 2 times the health plan limit, member meets **both** of the following (a and b):
   a. Failure of TWO prophylactic migraine medications, unless clinically significant adverse effects are experienced or all are contraindicated *(see Appendix B)*;
   b. Member is being treated by or in consultation with a neurologist, headache, or pain specialist;
9. Dose does not exceed the FDA-approved maximum dose *(see Section V)*.

Approval duration: 12 months or duration of request, whichever is less

B. Migraines – Non-Oral Agents (must meet all)**:**
1. Diagnosis of migraine headaches;
2. Request is for a non-oral agent (i.e., nasal spray or injectable);
3. Member meets the following age requirements (a or b):
   a. For Zomig, Imitrex nasal spray: Age ≥ 12 years;
   b. For Imitrex injection, Onzetra Xsail, Tosymra, Zembrace SymTouch: Age ≥ 18 years;
4. Failure of sumatriptan (Imitrex) nasal spray, unless contraindicated or clinically significant adverse effects are experienced;
5. Member meets one of the following (a or b):
   a. Failure of at least TWO oral generic $5HT_1$-agonist migraine medications (e.g., almotriptan, naratriptan, rizatriptan/rizatriptan ODT, or sumatriptan succinate) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;
   b. Member is unable to use oral agents due to migraine-associated nausea;
6. For requests of monthly quantities > 2 kits per month (Imitrex injection, Zembrace SymTouch), > 6 nasal spray devices per month (Imitrex, Tosymra, Zomig nasal spray), or > 1 kit per month (Onzetra Xsail), member meets both of the following (a and b):
   a. Failure of at least TWO prophylactic migraine medications at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated *(see Appendix B for examples)*;
   b. Member is being treated by or in consultation with a neurologist, headache, or pain specialist;
7. Dose does not exceed the following:
   a. Imitrex nasal spray: 40 mg per day;
   b. Tosymra nasal spray: 30 mg per day;
   c. Zomig nasal spray: 10 mg per day;
   d. Imitrex injection, Zembrace SymTouch: 12 mg per day;
   e. Onzetra Xsail (i and ii):
      i. 44 mg per day;
      ii. 4 capsules per day.

Approval duration:
Imitrex, Tosymra, and Zomig nasal spray – 12 months or duration of request, whichever is less
All others – 6 months or to the member's renewal period, whichever is longer

C. Cluster Headaches (must meet all)**:**
1. Diagnosis of cluster headaches;
2. Request is for Imitrex nasal spray, Imitrex injection, or Zomig;
3. Prescribed by or in consultation with a neurologist, headache, or pain specialist;
4. Age ≥ 18 years;
5. Dose does not exceed either of the following (a, b, or c):
   a. Imitrex nasal spray: 40 mg per 24 hours;
   b. Imitrex injection: 12 mg per day;
   c. Zomig: 10 mg per day.

Approval duration:
Nasal spray – 12 months or duration of request, whichever is less
Injection – 6 months or to the member's renewal period, whichever is longer

D. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed the FDA-approved maximum dose *(see Section V)*.

Approval duration:
Oral formulations and nasal spray – 12 months or duration of request, whichever is less
Injection – 6 months or to the member's renewal period, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – CP.CPA.09 or evidence of coverage documents;
B. Management of hemiplegic or basilar migraines;
C. Prophylactic therapy of migraine.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
AAN: American Academy of Neurology
FDA: Food and Drug Administration
MAO: monoamine oxidase

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
naratriptan	One tablet (1 or 2.5 mg) PO at onset; can be repeated in 4 hours	5 mg/day
sumatriptan (Imitrex® nasal spray)	One spray (5 - 20mg) at onset into one nostril; can be repeated in 2 hours	40 mg/day
sumatriptan (Imitrex® tablets)	One tablet (25 -100mg) PO at onset; can be repeated in two hours	200 mg/day
rizatriptan (Maxalt®, Maxalt MLT® tablets)	One tablet (5 or 10 mg) PO at onset of migraine headache; can be repeated in two hours	30 mg/day

Preventive Therapies for Migraine		
Medication	**Dose**	**Dose Limit/ Maximum Dose**
Anticonvulsants such as: divalproex (Depakote®), topiramate (Topamax®), valproate sodium	**Migraine Prophylaxis** *Refer to prescribing information or Micromedex*	*Refer to prescribing information or Micromedex*
Beta-blockers such as: propranolol (Inderal®), metoprolol (Lopressor®)*, timolol, atenolol (Tenormin®)*, nadolol (Corgard®)*	**Migraine Prophylaxis** *Refer to prescribing information or Micromedex*	*Refer to prescribing information or Micromedex*

Preventive Therapies for Migraine		
Medication	**Dose**	**Dose Limit/ Maximum Dose**
Antidepressants/tricyclic antidepressants* such as: amitriptyline (Elavil®), venlafaxine (Effexor®)	**Migraine Prophylaxis** *Refer to prescribing information or Micromedex*	*Refer to prescribing information or Micromedex*
Rimegepant (Nurtec® ODT)	75 mg PO every other day	75 mg/dose
Erenumab-aaoe (Aimovig™)	70 mg SC once monthly Some patients may benefit from a dosage of 140 mg injected subcutaneously once monthly	140 mg/month
Galcanezumab-gnlm (Emgality®)	Loading dose: 240 mg SC once Maintenance dose: 120 mg SC once monthly	120 mg/month
Fremanezumab-vfrm (Ajovy®)	225 mg SC once monthly or 675 mg SC every three months	675 mg every 3 months
Eptinezumab-jjmr (Vyepti™)	100 mg IV every 3 months	300 mg every 3 months
Atogepant (Qulipta™)	10 mg, 30 mg, or 60 mg PO QD	60 mg/day
Rimegepant (Nurtec® ODT)	75 mg PO every other day	75 mg/dose
OnabotulinumtoxinA (Botox®)	Up to 5 Units IM per injection across up to 7 head/neck muscles for a total of up to 155 Units per treatment session	See dosing regimen

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - All triptans:
    - History of coronary artery disease or coronary vasospasm; symptomatic Wolff-Parkinson-White syndrome or other cardiac accessory conduction pathway disorders (except Maxalt); history of stroke, transient ischemic attack, or hemiplegic or basilar migraine, or peripheral vascular disease; ischemic bowel disease; uncontrolled hypertension; hypersensitivity.
    - Recent (within 24 hours) used of another 5-HT1 agonist (e.g., another triptan), or an ergotamine-containing medication.

- Relpax: within at least 72 hours of treatment with the following potent CYP3A4 inhibitors: ketoconazole, itraconazole, nefazodone, troleandomycin, clarithromycin, ritonavir or nelfinavir.
- Imitrex, Maxalt, RizaFilm, Tosymra, Treximet, Zomig: use concurrently or within 2 weeks of discontinuation of an MAO-A inhibitor or non-selective MAO inhibitor.
- Naratriptan, Imitrex, Onzetra, Treximet, Tosymra, Zembrace SymTouch: severe hepatic impairment.
- Naratriptan: severe renal impairment.
- Treximet: in the setting of CABG surgery; history of asthma, urticarial, other allergic type reactions, rhinitis, or nasal polyps syndrome after taking aspirin or other NSAID/analgesic drugs.
- RizaFilm: co-administration with propranolol.

- Boxed warning(s):
  - Treximet: risk of serious cardiovascular and gastrointestinal events
  - All other triptans: none reported

Appendix D: General Information

- The triptans should not be used for hemiplegic or basilar migraines due to an increased risk of stroke.
- AAN guidelines for cluster headaches support the use of Imitrex nasal spray for acute treatment (Level B). Per AAN, intranasal sumatriptan at a dose of 20 mg has been shown to be effective in the acute treatment of cluster headache. Zolmitriptan nasal spray (Level A) 5 mg and 10 mg and zolmitriptan oral (Level B) 5 mg and 10 mg are also recommended by AAN.
- According to AAN guidelines, verapamil, lithium and melatonin may be considered (Level C) for the prevention of cluster headaches.
- The AAN recommends that prophylactic migraine medications should be considered if the patient experiences 2 or more attacks per month that produce aggregate disability of 3 or more days/month.
- The AAN and the National Headache Foundation recommend that prophylactic migraine medications should be considered if one or more of the following are present: greater than 2 migraine headaches per week; migraines cause significant impairment in daily routine even with abortive treatment; contraindication to, adverse effects, overuse or failure of abortive migraine medications, presence of uncommon migraine condition (e.g., basilar migraine); or patient requesting prophylactic therapy.

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Almotriptan	6.25 to 12.5 mg PO QD May repeat dose in 2 hours	25 mg/24 hours
Eletriptan (Relpax)	20 or 40 mg PO QD May repeat dose in 2 hours	40 mg/dose 80 mg/24 hours
Frovatriptan (Frova)	2.5 mg PO QD May repeat dose in 2 hours	7.5 mg/24 hours
Naratriptan	1 or 2.5 mg PO QD May repeat dose in 4 hours	5 mg/24 hours

Drug Name	Dosing Regimen	Maximum Dose
Rizatriptan (Maxalt, Maxalt-MLT)	Adults: 5 or 10 mg PO QD May repeat dose in 2 hours Pediatrics: < 40 kg: 5 mg PO QD ≥ 40 kg: 10 mg PO QD	Adults: 30 mg/24 hours Pediatrics: 1 dose/24 hours
Rizatriptan oral film (RizaFilm)	Adults: 10 mg PO QD May repeat dose in 2 hours Pediatrics: ≥ 40 kg: 10 mg PO QD	Adults: 30 mg/24 hours Pediatrics: 10 mg/24 hours
Sumatriptan (Imitrex) tablet	25 to 100 mg PO QD May repeat dose in 2 hours	200 mg/24 hours
Sumatriptan nasal spray (Imitrex)	One spray (5-20 mg) intranasally at onset into one nostril May repeat dose in 2 hours	40 mg/24 hours
Sumatriptan nasal powder (Onzetra Xsail)	Migraines: 22 mg administered by use of one nosepiece (11 mg) in each nostril; may repeat after 2 hours	44 mg/day
Sumatriptan nasal spray (Tosymra)	Migraines: 10 mg intranasally into one nostril; may repeat after one hour	30 mg/24 hours
Sumatriptan succinate injection (Imitrex injection)	Migraines: One injection SC at onset; may repeat after one hour Cluster headaches: One injection SC at onset; may repeat after one hour	2 injections (12 mg)/24 hours
Sumatriptan auto-injector (Zembrace SymTouch)	Migraines: 3 mg dose SC at onset; may repeat for 3 additional doses separated by at least 1 hour	12 mg/day
Sumatriptan/naproxen (Treximet)	Adults 1 tablet (85 mg sumatriptan/500 mg naproxen) PO QD May repeat dose in 2 hours Pediatrics: 12 to 17 years of age 1 tablet (10 mg sumatriptan/60 mg naproxen) PO QD	Adults: 2 tablets (170 mg sumatriptan/1,000 mg naproxen)/24 hours Pediatrics: 12 to 17 years of age: 1 tablet (85 mg sumatriptan/500 mg naproxen)/24 hours
Zolmitriptan (Zomig and Zomig ZMT)	1.25 or 2.5 mg PO QD May repeat dose in 2 hours	5 mg/dose 10 mg/24 hours

Drug Name	Dosing Regimen	Maximum Dose
Zomig nasal spray (zolmitriptan)	Adults and Pediatrics 2.5 mg intranasally into one nostril May repeat dose in 2 hours	5 mg/dose 10 mg/24 hours

VI. Product Availability

Drug	Availability
Almotriptan	Tablets: 6.25 mg (package size 6), 12.5mg (package size 12)
Eletriptan (Relpax)	Tablets: 20 mg (package size 6), 40 mg (package size 6, 12)
Frovatriptan (Frova)	Tablet: 2.5 mg (package size 9)
Naratriptan	Tablets: 1 mg, 2.5 mg (package size 9)
Rizatriptan (Maxalt)	Tablets: 5 mg, 10 mg (package size 6, 12, 18)
Rizatriptan orally disintegrating (Maxalt MLT)	Tablets: 5 mg, 10 mg (package size 3, 6, 9, 12, 18)
Rizatriptan (RizaFilm)	Oral film: 10 mg (package size 6, 12, 18)
Sumatriptan (Imitrex)	Tablets: 25 mg, 50 mg, 100 mg (package size 9)
Sumatriptan nasal spray (Imitrex Nasal)	Nasal spray devices: 5 mg, 20 mg (package size 6)
Sumatriptan nasal powder (Onzetra Xsail)	Capsule in disposable nosepiece: 11 mg (kit contains 8 doses)
Sumatriptan nasal spray (Tosymra)	Nasal spray, single-dose: 10 mg (package size 6)
Sumatriptan succinate solution auto-injector (Imitrex STATdose System)	Each package contains 1 pen with 2 prefilled single dose syringe cartridges: 4 mg/0.5 mL, 6 mg/0.5 mL
Sumatriptan succinate solution cartridge (Imitrex injection cartridge)	2 prefilled syringe cartridges for refill: 4 mg/0.5 ml, 6 mg/0.5 mL
Sumatriptan succinate (Imitrex injection)	Single-dose vials: 6 mg (6 mg/0.5 mL) in cartons of 5 vials
Sumatriptan auto-injector (Zembrace SymTouch)	Prefilled, single-dose auto-injector: 3 mg/0.5 mL (4 auto-injectors per carton)
Sumatriptan/naproxen (Treximet)	Tablet: 85 mg sumatriptan/500 mg naproxen sodium (package size 9, 12), 10 mg sumatriptan/60 mg naproxen sodium (package size 9)
Zolmitriptan (Zomig)	Tablets: 2.5 mg (package size 6), 5 mg (package size 3)
Zolmitriptan nasal spray (Zomig Nasal Spray)	Nasal sprays: 2.5 mg, 5 mg (package size 6)
Zolmitriptan orally disintegrating (Zomig ZMT)	Tablets: 2.5 mg (package size 6), 5 mg (package size 3)

VII. References

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2020 annual review: no significant changes; modified multiple drug trial language to state unless all are contraindicated; updated limitation of use and contraindications by product; references reviewed and updated.	07.23.20	11.20
4Q 2021 annual review: no significant changes; updated therapeutic alternatives table to include additional migraine prophylaxis therapies (e.g., CGRPs, Botox); references reviewed and updated.	07.22.21	11.21
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	09.27.21	02.22
4Q 2022 annual review: no significant changes; added Nurtec ODT, Qulipta, and Vyepti to therapeutic alternatives table; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	07.13.22	11.22
RT4: added Rizafilm to policy; removed Sumavel Dosepro from policy as it is no longer commercially available; in Section IA, clarified for non-preferred agents failure of two formulary "generic" 5HT1-agonist migraine medications.	04.21.23	
4Q 2023 annual review: no significant changes; removed references to Axert which is no longer commercially available; references reviewed and updated.	06.23.23	11.23
4Q 2024 annual review: no significant changes; removed references to Amerge as branded product is discontinued; references reviewed and updated.	07.12.24	11.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted

standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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