Health Technology Briefing
April 2024

Telmisartan-amlodipine-indapamide for treating hypertension

Company/Developer	George Health (George Medicines PTY Limited)

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 30368	NICE ID: Not Available	UKPS ID: 674895[a]

Licensing and Market Availability Plans

Currently in phase II/III clinical trials.

Summary

Telmisartan-amlodipine-indapamide is in development for the treatment of Hypertension. Hypertension is characterised by persistently high blood pressure. When a person's blood pressure is too high, it puts extra strain on the blood vessels, heart and other organs, such as the brain, kidneys and eyes. The causes of high blood pressure are not always clear, but the risks are increased by factors such as being overweight, eating too much salt and lack of exercise. In about 1 in 10 cases of hypertension, there is an underlying cause, such as a health condition or a specific medication. Hypertension often does not have symptoms but if someone has very high blood pressure then they may experience headaches, blurred or double vision, regular nosebleeds, or shortness of breath. Hypertension is a prevalent (common) condition that can be serious if not treated. The use of combination therapies for hypertension has the potential to improve blood pressure control to a greater extent than monotherapies.

Telmisartan-amlodipine-indapamide is a single-pill, fixed-dose combination therapy currently in clinical development for treating high blood pressure. The three different agents making up this treatment work by blocking substances that cause blood vessels to tighten, relaxing blood vessels, and reducing the amount of water in the body, respectively. If licensed, telmisartan-amlodipine-indapamide will offer an additional treatment option for adults with hypertension.

[a] Information provided by George Medicines but did not retrieve a result when searched on the UK Pharmascan database. This is because the UKPS record was newly created at the time of this technology briefing's submission.

Proposed Indication

First-line treatment of adults with a likely diagnosis of hypertension.[1-3]

Technology

Description

Telmisartan-amlodipine-indapamide (GMRx2) is a single-pill, multi-mechanism, triple combination therapy for treating hypertension that comprises the commonly used hypertension medicines: telmisartan, amlodipine and indapamide.[1,3] Telmisartan is an angiotensin II receptor blocker (ARB). Angiotensin II is a powerful vasoconstrictor hormone (a substance that narrows blood vessels). By blocking the receptors to which angiotensin II normally attaches, telmisartan stops the hormone from narrowing the blood vessels, allowing the blood vessels to widen for blood pressure to drop.[4] Amlodipine is a calcium channel blocker (CCB) and inhibits the influx of calcium ions into cardiac and vascular smooth muscle. It dilates the peripheral arterioles thereby reducing the total peripheral resistance against which the heart works.[5] Indapamide is a non-thiazide sulfonamide with an indole ring, belonging to the diuretic family.[6] It is intended for lowering arterial blood pressure and as an adjuvant drug for treating oedema caused by cardiac insufficiency.[7]

Telmisartan-amlodipine-indapamide is currently in phase III studies (NCT04518293, NCT04518306) at varying doses of its constituting drugs in order to treat hypertension.[1,2] In the recently completed phase III trial (NCT04518306), two different doses of telmisartan-amlodipine-indapamide were administered orally and compared with a placebo during a 4-week period.[1] In the other recently completed phase III trial (NCT04518293) two different doses of telmisartan-amlodipine-indapamide were compared to the three possible dual combinations.[2]

Key Innovation

Hypertension is a growing global health problem and is predicted to affect 1.56 billion people by 2025.[8] More than 70% of adults treated for primary hypertension will eventually require at least two antihypertensive agents, either initially as combination therapy or as add-on therapy if monotherapy and lifestyle modifications do not achieve adequate blood pressure control.[9] However, recommended fixed-dose combinations of an ARB, CCB, and a thiazide-like diuretic are presently indicated only for people currently receiving all three agents, or those uncontrolled on two of these agents.[10,11] The National Institute for Health and Care Excellence (NICE) currently only recommends triple combination therapy as step 3 treatment for people with hypertension with or without diabetes uncontrolled on two agents.[12]

Compared with monotherapy, initial combination therapy improves the average decrease in blood pressure and achieves blood pressure control faster, with similar tolerability.[9] In recent years there has been interest in low-dose combination therapy of three or more drugs, with evidence indicating that low-dose treatment of multiple drug classes may achieve greater blood pressure control without increasing adverse effects.[11] Telmisartan-amlodipine-indapamide fixed-dose combination therapy has the potential to provide an optimal balance of increased efficacy and patient adherence and reduced side effects compared with current treatments.[3] If licensed, telmisartan-amlodipine-indapamide will offer an additional treatment option for adults with hypertension.

Regulatory & Development Status

Telmisartan-amlodipine-indapamide does not currently have marketing authorisation in the EU/UK for any indication.
Telmisartan-amlodipine-indapamide is not in phase III/II clinical development for any indications.[13]

Patient Group

Disease Area and Clinical Need

Hypertension is characterised by persistently high arterial blood pressure.[14] The blood pressure reading for hypertension is considered to be from 140/90mmHg or more if the reading was taken at a pharmacy, GP surgery or clinic (or an average of 135/85mmHg if it was taken at home).[15] If a person's blood pressure is too high, it puts extra strain on the blood vessels, heart and other organs, such as the brain, kidneys and eyes.[15] In most cases, there are no exact causes of hypertension, but in about 1 in 10 cases high blood pressure happens because of an underlying health condition, such as kidney disease or diabetes, or taking certain medicines, such as the contraceptive pill or steroids.[16] Factors that can increase the risk of having high blood pressure include being overweight, too much salt intake, not eating enough fruit and vegetables, not doing enough exercise, drinking too much alcohol, coffee or other caffeine-based drinks, smoking, stress and being over 65 years old.[15] Hypertension does not usually cause any obvious symptoms, but in rare cases where a person has very high blood pressure, they can experience: blurred vision, nose bleeds, shortness of breath, chest pain and headaches.[17]

It is estimated that 11.8 million adults in England had hypertension in 2017, equating to around 26.2% of the population, or approximately one in four adults.[18] In England in 2022-23, there were 42,901 finished consultant episodes (FCE) and 35,526 admissions for essential (primary) hypertension (ICD-10 code I10) which resulted in 35,037 FCE bed days and 3033 day cases.[19]

Recommended Treatment Options

NICE recommend lifestyle interventions as treatments for hypertension, which can include advising patients on healthy diets, regular exercise and discouraging consumption of alcohol and caffeine-rich products. Additionally, NICE recommend offering antihypertensive drug treatments such as angiotensin-converting enzyme (ACE) inhibitors, ARBs, CCBs or thiazide-like diuretics as monotherapy or combination therapy, depending on treatment stage, in addition to lifestyle advice.[12]

Clinical Trial Information

Trial	**GMRx2_PCT**, NCT04518306; Efficacy and Safety of GMRx2 (a Single Pill Combination Containing Telmisartan/Amlodipine/Indapamide) Compared to Placebo for the Treatment of Hypertension **Phase III** - Completed **Location(s):** UK, USA, and other countries **Study completion date**: October 2023
Trial Design	Randomised, parallel-assignment, quadruple-blind, placebo-controlled
Population	N = 295 (actual); adults aged 18 or over with a likely diagnosis of hypertension
Intervention(s)	Treatment groups: • Triple ¼ (GMRx2): oral telmisartan 10 mg/amlodipine 1.25 mg/indapamide 0.625 mg

	• Triple ½ (GMRx2): oral telmisartan 20 mg/amlodipine 2.5 mg/indapamide 1.25 mg
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome: Difference in change in home seated systolic blood pressure from baseline to week 4 [Time Frame: 4 weeks] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Trial	**GMRx2_ACT**, NCT04518293, 2020-004196-40; Efficacy and Safety of GMRx2 (a Single Pill Combination Containing Telmisartan/Amlodipine/Indapamide) Compared to Dual Combinations for the Treatment of Hypertension **Phase III** – Completed **Location(s)**: two EU countries, UK, USA, and other countries **Study completion date**: September 2023
Trial Design	Randomised, parallel assignment, active-controlled, quadruple-blind
Population	N = 1385 (actual); adults 18 years and older with hypertension, receiving 0, 1, 2 or 3 BP lowering medicines; eligible if, in the week prior to the randomisation visit, had a home seated mean systolic blood pressure 110 to 154 mmHg.
Intervention(s)	Experimental group: telmisartan 20 mg/amlodipine 2.5 mg/indapamide 1.25 mg. At week 6 visit, forced up-titration to telmisartan 40 mg/amlodipine 5 mg/indapamide 2.5 mg
Comparator(s)	Group 1: Telmisartan 20 mg/amlodipine 2.5 mg. At week 6 visit, forced up-titration to telmisartan 40 mg/amlodipine 5 mg Group 2: Telmisartan 20 mg/indapamide 1.25 mg. At week 6 visit, forced up-titration to telmisartan 40 mg/indapamide 2.5 mg Group 3: Amlodipine 2.5 mg/indapamide 1.25 mg. At week 6 visit, forced up-titration to amlodipine 5 mg/indapamide 2.5 mg
Outcome(s)	Primary outcome: Difference in change in home systolic blood pressure from baseline to week 12 [Time Frame: 12 weeks] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of telmisartan-amlodipine-indapamide is not yet known. The NHS indicative price of Telmisartan 20mg is £9.99 for a pack of 28 tablets.[20] Amlodipine 2.5mg costs £6 for a pack of 28 tablets, while Indapamide costs £0.85 for a pack of 28 2.5mg tablets.[21,22]

Relevant Guidance

NICE Guidance

- NICE clinical guideline. Hypertension in adults: diagnosis and management (NG136). November 2023.
- NICE quality standard. Hypertension in adults (QS28). September 2015.

NHS England (Policy/Commissioning) Guidance

- No relevant guidance identified.

Other Guidance

- Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. 2020.[23]
- Williams B, Mancia G, Spiering W, Rosei EA, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH). 2018.[24]
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Additional Information

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