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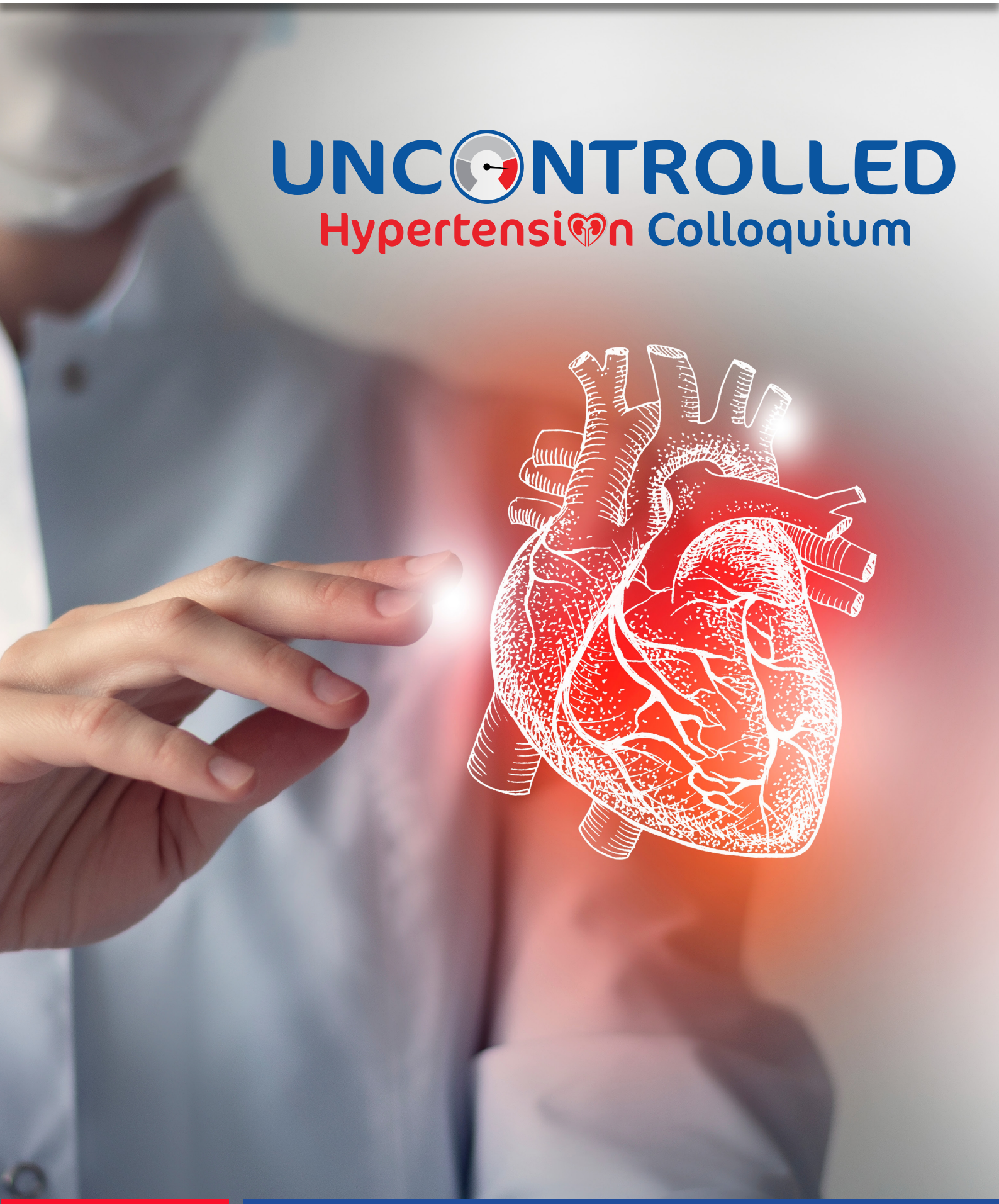
UNCONTROLLED
Hypertension Colloquium



Synopsis

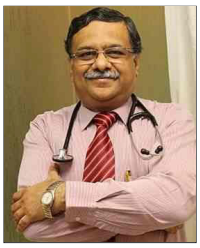
Resistant hypertension

Dr. Thomas Unger,
Professor Emeritus. of Pharmacology and Experimental Medicine

Hypertension is one of the leading risk factors for mortality across the world.[4] Hypertension is a risk factor for several complications, including myocardial infarction and left ventricular hypertrophy, which can lead to heart failure and death when combined with other risk factors such as smoking, obesity, and diabetes.[5]

One in 5 hypertensives in India has resistant hypertension. Prevalence of resistant hypertension is high in secondary-care practice in India. It is significantly greater among older patients (> 60 yrs) and women.[6] According to the 2020 ISH guidelines, suspect resistant hypertension if office BP is greater than 140/90 mmHg on treatment with at least three antihypertensives (at optimal or maximally tolerated doses), including a diuretic.[7] It is critical to confirm treatment resistance, exclude pseudo resistance, and assess for secondary hypertension when evaluating resistant hypertension.[8] To conclude, when three drugs are required to control BP, a combination of an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB), a calcium-channel blocker (CCB), and a thiazide diuretic is used. The fourth medication can be used to treat resistant hypertension. Alpha-1-blockers are frequently used in the treatment of resistant hypertension due to their improved safety and tolerability.[9]

Context setting



Dr. Bhupen Navinchandra Desai,
Interventional Cardiologist

One of the most significant challenges in the diagnosis and management of hypertension in India is a lack of awareness.[1,1A] Various measures can be adopted to address these challenges such as[2]:

- Driving awareness about the dangers of uncontrolled hypertension among patients, professionals, and policymakers
- Efficient patient education
- Effective use of the multidisciplinary team
- Encouraging patients to take responsibility for their own CV health and promote self-monitoring of BP
- Simplifying treatment strategies
- Taking a leadership role in communities, professions, and society

It is critical to rule out secondary causes of hypertension such as obstructive sleep apnea, primary aldosteronism, chronic kidney disease, renal artery stenosis, etc.[3]

Management of uncontrolled hypertension with co-morbidities and role of alpha blockers

Dr. Jamshed J. Dalal,
Interventional Cardiologist

According to the Great India Blood Pressure Survey, "one out of every five young Indian adults has high BP." Emphasis should be placed on screening individuals for hypertension beginning at the age of 18, as this is the age at which most countries begin monitoring BP.[10,10A]

Hypertension is prevalent in 85% to 95% of patients with stages 3-5 chronic kidney disease (CKD).[11] Uncontrolled hypertension increases the risk of several co-morbidities like heart attack, heart failure, kidney disease, etc;[11A] still only 12% of India's estimated 220 million hypertensive people have their BP under control.[12]

ASCOT trial showed that alpha blockers had beneficial effects, with doxazosin GITS recipients showing lower BP, lower levels of triglycerides and cholesterol and no increase in the incidence of heart failure.[13]

Indian as well as international guidelines such as ISH and NICE have incorporated alpha-blockers as the therapy for hypertension but as the last choice.[14,15,16]

Patients with resistant hypertension must take alpha-blockers to lower BP.[9] Patients with recurrent hyperkalemia in whom RAS blockers and spironolactone cannot be considered, those with benign prostatic hyperplasia who are 50 years of age or older, may benefit from additional therapy with alpha-blockers.[13]

Alpha-blockers should be taken into consideration in patients with CKD and potassium levels of 5 mEq/L.[13] It has been noticed that taking alpha-blockers before bedtime lowers the morning rise in blood pressure, which lowers the risk of stroke and myocardial infarction.[13] Thus, alpha-blockers are particularly preferred for managing uncontrolled BP in individuals with comorbidities such as diabetes, heart failure, renal insufficiency, BPH, gout, dyslipidemia, and more.[17] Prazosin with GITS release ensures more than 40% drug release the in first 12 hours, resulting in smoother BP control throughout the dosing interval of 24 hours.[18]

Hypertensive patient with CKD – Experience with use of Alpha 1 blocker

Dr. Manish Jain
Consultant Nephrologist

A case was discussed of a 65-year-old male with known a history of DM, HTN since 15-16 years, and CKD stage 5 on maintenance hemodialysis. The patient is currently on multiple antihypertensive - Amlodipine 10 mg twice daily, Clonidine 0.2 mg thrice a day, Metoprolol 50 mg once a day. He has been observing consistently high BP readings at home ranging between 170-180 mmHg systolic.

Patient was started on Telmisartan for intradialytic hypertension and his BP readings improved.

A few days, later patient was brought to the hospital with bradycardia and was found to have potassium levels of 6.7 mEq/L. In view of hyperkalemia, Telmisartan was stopped but the patient developed intradialytic hypertension.

As CKD advances, diuretics cannot be administered. Due to the high likelihood that the patient will develop anuria from CKD, diuretics are not necessary. CCBs are also acting centrally, making them inefficient. The patient was then started on prazosin 2.5 mg twice daily and gradually increased to 5 mg. This resulted in better BP control during home BP readings. His current BP is 130/80 mmHg.

Alpha-blocker is the mainstay of therapy for nephrologists in stages 3 and 4. As per India data from SEEK study- the prevalence of CKD was observed to be 17.2% with ~6% having CKD stage 3 or worse.[19]

Alpha-blockers not only control BP in patients with CKD but also reduce the incidence of proteinuria.[13,17,20]

Alpha-blockers are preferred in renal transplant recipients too as:

- The standing BP reduced[21]
- No significant influence on plasma creatinine[21,22]
- No further deterioration of renal function[21]
- No variations in total cholesterol and triglyceride, glucose or uric acid[21]
- It is well-tolerated and efficient, not increasing metabolic AEs[22]

Prazosin must be administered with special care during dialysis because it is largely bound to plasma proteins, is relatively stable during dialysis, and is primarily metabolized and excreted by the liver.[23,24] Alpha-blockers have good antihypertensive efficacy in hypertensive CKD patient[20] and beneficial effects on endothelial function[20] and decrease sympathetic overactivity.[13,17]

Hypertensive patient with diabetes, dyslipidaemia with uncontrolled hypertension on ACEI/ ARB + diuretics -Experience with use of Alpha 1 blocker

Dr. Sunil Rameshchandra Dube,
Consultant Physician

A case of a 62-year-old male retired person was discussed who came with complaints of polyuria with increased frequency at night, blurred vision, easy fatigability, and knee joint pain. His pulse was 60 beats/min and BP was 158/92 mmHg. The patient has a medical history of hypertension since 11 years, diabetes since 10 years, osteo arthritis of the knees, and dyslipidaemia. He has been hospitalized for hyponatremia too. His present medications include Telmisartan 40 mg OD, Amlodipine 5 mg BD, Chlorthalidone 6.25 mg, Dapagliflozin 10 mg, Linagliptin 5 mg, Glimepiride 2 mg, Metformin 1500 mg, Rosuvastatin 20 mg, and Vitamin supplement. Lab reports showed well-controlled diabetes and cholesterol level. He had an eGFR of 57 ml/min/1.73m^2 suggestive of CKD stage 3 and renal dysfunction. Besides this high uric acid and hyperkalemia were noted. ECG suggested left ventricular hypertrophy. Ophthalmic examination revealed evidence of diabetic and hypertensive retinopathy.

Management considerations for this patient:

- **Beta-blockers:** There was no compelling indication such as IHD to initiate and pulse too was 68/min.
- **MRA:** Cannot be considered due to renal dysfunction and hyperkalemia.
- **ACEI:** This too was not considered as the patient was on telmisartan.
- **Alpha- blockers:** Prazosin 2.5 mg was initially added and stepped up to 5 mg OD at night.

Other medications: Amlodipine 5 mg BD and telmisartan 40 mg were continued. Diuretics were stopped due to past hospitalization for hyponatremia, raised uric acid and the patient was also on SGLT2i.

After 4 weeks of follow-up - His nocturnal frequency of urination improved. His BP was 130/80 mmHg with no postural hypotension. Home BP measurement was 126/76 mmHg on average and ambulatory BP measurement too confirmed well-controlled BP.

In cases of uncontrolled hypertension where patients did not respond to or were intolerant of the initial regimens, alpha-blockers have a significant role to play as a third-line agent.[20]

Patients with BPH should think about taking alpha-blockers because they help to alleviate the lower urinary symptoms of prostate hypertrophy.[9]

Alpha-blockers is preferred for managing uncontrolled blood pressure in individuals **with comorbidities such as diabetes, heart failure, renal insufficiency, BPH, gout and dyslipidemia.**[17]

Q A Panel Discussion (Q and A)

Do alpha-blockers increase the risk of heart failure and postural hypotension?

A low dose of an alpha-blocker will be beneficial because it lowers the incidence of postural hypotension and its associated symptoms and does not increase the risk of heart failure.[20]

Can existing alpha-blockers be stopped in people with BPH while starting prazosin?

Prazosin is typically started at low doses that are sufficient to lower blood pressure, but the low doses may not be enough to cause structural or symptomatic changes in BPH patients. Existing alpha-blockers may be stopped if high doses of prazosin are effective in controlling BPH symptoms.[25]

MINIPRESS® XL GITS Tablets

Abbreviated Prescribing Information / Summary of Product Information

GENERIC NAME: Prazosin Hydrochloride GITS Tablets **PRESENTATION:** Each film-coated GITS tablet (controlled release tablet) contains Prazosin Hydrochloride I.P equivalent to 2.5 or 5 mg prazosin. All strengths/presentations mentioned in this document might not be available in the market. **INDICATION(s):** Hypertension-Prazosin hydrochloride GITS is indicated in the treatment of all grades of essential (primary) hypertension and of all grades of secondary hypertension of varied etiology. It can be used as the initial and sole agent, or it may be employed in a treatment program in conjunction with a diuretic and/or other antihypertensive drugs as needed for proper patient response. Benign Prostatic Hyperplasia (BPH)-Prazosin hydrochloride GITS is indicated as an adjunct in the symptomatic treatment of urinary obstruction caused by benign prostatic hyperplasia. It is also of value in patients awaiting prostatic surgery. **DOSAGE AND ADMINISTRATION:** Prazosin hydrochloride GITS can be taken with or without food. The GITS tablets could be swallowed whole with a sufficient amount of liquid. Patients should not chew, divide, or crush the tablets. The dose of prazosin hydrochloride GITS should be adjusted according to the patient's individual blood pressure response. For hypertension, the initial dose is 2.5 mg given once daily, may be increased gradually as clinically indicated to 20 mg given in once daily doses. For Benign Prostatic Hyperplasia, starting dose is 2.5 mg given once daily for a period of 3 to 7 days. The usual maintenance dosage is 5 mg given once daily which should not be exceeded. Oral administration. Fertility, pregnancy and lactation- Animal studies have shown that prazosin hydrochloride may alter fertility. There are no adequate and well controlled studies which establish the safety of prazosin hydrochloride in pregnant women. Prazosin hydrochloride should be used during pregnancy only if in the opinion of the physician the potential benefit justifies the potential risk to the mother and fetus. Prazosin hydrochloride has been shown to be excreted in small amounts in human milk. Caution should be exercised when prazosin hydrochloride is administered to nursing mothers. Use in Renally Impaired Patients-Prazosin hydrochloride GITS can be used with safety in hypertensive patients with impaired renal function. Use in Children-Prazosin hydrochloride GITS is not recommended for the treatment of children under the age of 12 years since safe conditions for its use have not been established. **CONTRAINDICATIONS:** Prazosin hydrochloride GITS is contraindicated in patients with known sensitivity to quinazolines, prazosin hydrochloride, or any of the inert ingredients. **WARNING AND PRECAUTIONS:** When used for hypertension: a very small percentage of patients may respond abruptly, in exaggerated manner to the initial dose of prazosin hydrochloride. Postural hypotension has been reported, particularly with commencement of therapy. This is readily avoided by initiating treatment with a low dose, and with small increases in dosage during the first 1 to 2 weeks of therapy. This effect, when observed, is not related to the severity of hypertension, is self-limiting and in most patients does not recur after the initial period of therapy or during subsequent dose titration steps. When instituting therapy with any antihypertensive agent, the patient should be advised how to avoid symptoms resulting from postural hypotension and what measures to take should they develop. The patient should be cautioned to avoid situations where injury could result should dizziness or weakness occur during the initiation of prazosin hydrochloride therapy. Priapism: Since marketing, cases of prolonged erection and priapism have been reported with alpha-1 blockers, including prazosin. If an erection persists for more than 4 hours, the patient should immediately consult a doctor. If the priapism is not treated immediately, penile tissue lesions and permanent impotence may result. When used for BPH: Prazosin decreases peripheral vascular resistance; careful monitoring of blood pressure, during initiation or adjustment of the dose of Minipress® XL, is suggested. Markedly reduced GI retention times of prazosin hydrochloride GITS may influence the pharmacokinetic profile and hence the clinical efficacy of the drug. As with any other nondeformable material, caution should be used when administering prazosin hydrochloride GITS in patients with preexisting severe gastrointestinal narrowing (pathologic or iatrogenic). Patients should not be concerned if they occasionally notice in their stool something that looks like a tablet. In prazosin hydrochloride GITS the medication is contained within a nonabsorbable shell that has been specially designed to slowly release the drug so the body can absorb it. When this process is completed, the empty tablet is eliminated from the body. **DRUG INTERACTIONS:** Addition of a diuretic or other antihypertensive agent to prazosin hydrochloride has been shown to cause an additive hypotensive effect. Concomitant administration of prazosin hydrochloride GITS with a PDE-5 inhibitor should be used with caution as it may lead to symptomatic hypotension in some patients. False-positive results may occur in screening tests for pheochromocytoma (urinary vanillylmandelic acid [VMA] and methoxyhydroxyphenyl glycol [MHPG], urinary metabolites of norepinephrine) in patients who are being treated with prazosin hydrochloride. **OVERDOSE:** Should overdosage lead to hypotension, support of the cardiovascular system is of first importance. Restoration of blood pressure and normalization of heart rate may be accomplished by keeping the patient in the supine position. If this measure is inadequate, shock should first be treated with volume expanders. If necessary, vasopressors should then be used. Renal function should be monitored and supported as needed. **ADVERSE REACTION:** Lack of energy, weakness (asthenia), dizziness, headache, nausea, palpitations, drowsiness are most common reactions. In addition, diaphoresis, dry mouth, flushing, priapism, allergic reaction, fever, malaise, pain, angina pectoris, edema, hypotension, orthostatic hypotension, syncope, paresthesia, vertigo, positive ANA titer, gynecomastia, abdominal discomfort, constipation, diarrhea, pancreatitis, vomiting, tinnitus, bradycardia, tachycardia, liver function abnormalities arthralgia depression, hallucinations, impotence, insomnia, nervousness, dyspnea, epistaxis, nasal congestion, alopecia, pruritus, rash, lichen planus, urticaria, incontinence, urinary frequency, vasculitis, blurred vision, reddened sclera, eye pain have been reported. **PHARMACEUTICAL PRECAUTIONS:** Store below 30°C. Shelf Life- MINIPRESS XL tablets 2.5 mg,5 mg: 36 months.

REFERENCE: LPDMXL042017

DATE OF THIS DOCUMENT:8 October 2021

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