

Clinical Trial Summary

Study to evaluate two new gliclazide MR 120 mg tablets in healthy participants

Full scientific title: A single-dose, randomized, open-label, crossover, exploratory bioavailability study in healthy volunteers of two formulations of gliclazide MR tablets 120 mg (I.R.I.S.) and two Diamicron® MR tablets 60 mg (I.R.I.S.) under fasting and fed conditions and oral solution of 60 mg Gliclazide (I.R.I.S.) under fasting conditions

We thank all the participants who took part in the study. Clinical study participants are very important for making progress in science, for the benefit of patients.

This document is a summary of the study. It is written for a general audience.

Researchers need many studies to decide which medicines work the best and are the safest for patients. For medical science to progress, many studies involving patients are running all around the world. This summary only shows the results from this one study. Other studies, evaluating the same drug, may find different results. You should not change your current treatment based on the results of this single study or other studies. If you have any questions about this study and/or your treatment, please talk to your doctor.

Therapeutic area:
Endocrine
disorders

Disease:
Diabetes

Study phase:
Phase 1

Final version
20 Aug 2024

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9. Are there plans for further studies?
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1 Why was this study done?

Gliclazide is a medicine that reduces blood sugar levels. It is used in a certain form of diabetes (type 2 diabetes mellitus) in adults, when diet, exercise and weight loss alone are not enough to keep blood sugar at the correct level.

Diabetes is a disease that occurs when the levels of blood sugar is too high. In type 1 diabetes, the body doesn't make insulin (hormone that lowers the level of sugar in the blood). In type 2 diabetes, the body doesn't make enough insulin or can't use it as well as it should.

Gliclazide is available under several names including Diamicron® modified release (MR). It is already available in Europe and in many other countries around the world as MR tablets of 30 and 60 mg. Modified release tablet means that the active drug is released over several hours to maintain a constant amount of drug in the blood.

Gliclazide MR daily dose may vary from 30 mg to 120 mg. Currently, the patients requiring the highest dose of 120 mg should take 2 tablets of gliclazide MR 60 mg as a single dose at breakfast time. The availability of a 120 mg tablet would simplify the treatment. This may help the patients to stick to their treatment.

For this purpose, researchers are developing a new MR tablet containing 120 mg of gliclazide. The new tablet is designed in a way so that gliclazide gets absorbed in the body gradually and has a longer lasting action.

The aim of this study was to test if 3 different forms (fast, medium and slow release tablets) of 2 formulations of gliclazide MR 120 mg tablets (tablets A and B) were processed by the body of healthy participants in the same way as 2 Diamicron® MR 60 mg tablets.

Blood samples were collected from the participants to check how gliclazide was absorbed into the participants' bodies and moved through the blood. This is called "bioavailability". Bioavailability was tested under 2 conditions:

- With an empty stomach (fasting conditions).
- After eating a meal (fed conditions).

2 When and where did this study take place?

When did the study take place?

- This study started in November 2023.
- It ended in December 2023.

Where did the study take place?

The study took place in Portugal.

3 Who participated in the study?

Which participants were included in the study?

To take part, participants had to be:

- Male or female between 18 to 50 years of age.
- Healthy with no previous history of certain diseases as assessed by the research doctor.
- Within the set weight and build criteria.
- Non-smoker for at least 3 months before starting the study.

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How many participants took part in the study?

A total of 68 participants took part in the study: 24 women and 44 men.

How old were the participants?

The average age of the participants was 33 years. The youngest participant was 20 years old and the oldest was 48 years old.

4 Which treatments did the participants receive?

Gliclazide MR 120 mg tablets A and B are the test drugs that the researchers wanted to learn more about. Tablets A and B exist in 3 forms:

- Fast release form: gliclazide is released rapidly from the tablet, so absorbed in the body at rapid speed.
- Medium release form: gliclazide is released at medium speed from the tablet, so absorbed in the body at a medium speed.
- Slow release form: gliclazide is released at slow speed from the tablet, so absorbed in the body at a slow speed.

Diamicron® MR 60 mg (containing 60 mg of gliclazide) is used as the standard drug to compare bioavailability of gliclazide MR 120 mg tablets.

Gliclazide solution was also used as a standard drug with which the tablets may be compared. Gliclazide is absorbed very rapidly into the blood when given as a gliclazide solution.

The study was divided in 3 groups. Each participant could only be assigned to one group.

Each participant from groups 1 and 2 received the following drugs (each one separately) in fasting conditions (empty stomach):

- Gliclazide solution.
- Diamicron® MR 60 mg (2 tablets).
- Gliclazide MR 120 mg (tablet A **or** tablet B, one tablet):
 - Fast release form.
 - Medium release form.
 - Slow release form.

Each participant from group 3 received the following drugs (each one separately) in fed conditions (after a meal):

- Diamicron® MR 60 mg (2 tablets).
- Gliclazide MR 120 mg medium release form (tablet A **and** tablet B, one tablet).

Participants took the drugs by mouth in a specific order. They took the drugs as a single-dose after an overnight fast of at least 10 hours (group 1 and 2) or after 30 minutes of eating a meal (group 3).

5 How was the study carried out?

The study is called a “randomised” and “open-label” study:

- “Randomised” means that the order in which the participant took the drug was determined by chance.
- “Open-label” means that both the participants and the research doctors knew which treatment was taken.

The participants got each drug as a single dose in the morning on an empty stomach (group 1 and 2) or after eating (group 3). Each participant received gliclazide solution (except group 3), Diamicron® MR and gliclazide MR 120 mg tablets in a specific order. There was a break of at least 7 days between

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the drugs. This break allows each study drug to be completely removed from the participants' bodies before taking the next study drug.

Total study duration for participants in group 1 and 2 was 63 days and in group 3 was 48 days.

The participants visited the doctors regularly. During the visits, the doctors collected information about the participants' health.

6 What were the side effects?

Side effects are unwanted medical events that the doctors think may be caused by the treatments in the study.

In this summary, we describe unwanted medical events thought to be caused by gliclazide solution, Diamicron® MR, and gliclazide MR 120 mg tablets fast release, medium release, and slow release. The results may be presented differently in other documents related to the study.

The tables below show the number of participants who had side effects in each group.

Among the 24 participants in group 1, 1 participant stopped the study before receiving gliclazide MR tablets A. So, the results below are presented on 23 participants for the treatment with gliclazide MR tablets A.

	Group 1				
	Gliclazide tablet A fast release (out of 23 participants)	Gliclazide tablet A medium release (out of 23 participants)	Gliclazide tablet A slow release (out of 23 participants)	Diamicron® MR (out of 24 participants)	Gliclazide solution (out of 24 participants)
Participants who had side effect(s)	10 (43%)	10 (43%)	5 (22%)	10 (42%)	13 (54%)
Participants who had serious* side effect(s)	0	0	0	0	0
Participants who stopped the treatment because of side effect(s)	0	0	0	0	0

**See definition of serious side effects below*

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	Group 2				
	Gliclazide tablet B fast release (out of 24 participants)	Gliclazide tablet B medium release (out of 24 participants)	Gliclazide tablet B slow release (out of 24 participants)	Diamicron® MR (out of 24 participants)	Gliclazide solution (out of 24 participants)
Participants who had side effect(s)	13 (54%)	14 (58%)	4 (17%)	14 (58%)	18 (75%)
Participants who had serious* side effect(s)	0	0	0	0	0
Participants who stopped the treatment because of side effect(s)	0	0	0	0	0

*See definition of serious side effects below

	Group 3		
	Gliclazide tablet A medium release (out of 20 participants)	Gliclazide tablet B medium release (out of 20 participants)	Diamicron® MR (out 20 participants)
Participants who had side effect(s)	16 (80%)	8 (40%)	14 (70%)
Participants who had serious* side effect(s)	0	0	0
Participants who stopped the treatment because of side effect(s)	0	0	0

*See definition of serious side effects below

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What were the types of side effects?

The tables below show the most common side effects reported in the study (reported by at least 2 participants).

	Group 1				
	Gliclazide tablet A fast release (out of 23 participants)	Gliclazide tablet A medium release (out of 23 participants)	Gliclazide tablet A slow release (out of 23 participants)	Diamicron® MR (out of 24 participants)	Gliclazide solution (out of 24 participants)
Low blood sugar level	8  (35%)	6  (26%)	2  (9%)	9  (38%)	9  (38%)
Headache	2  (9%)	6  (26%)	2  (9%)	5  (21%)	3  (13%)
Throbbing headache	0 	0 	0 	0 	3  (13%)

 = participants

	Group 2				
	Gliclazide tablet B fast release (out of 24 participants)	Gliclazide tablet B medium release (out of 24 participants)	Gliclazide tablet B slow release (out of 24 participants)	Diamicron® MR (out of 24 participants)	Gliclazide solution (out of 24 participants)
Low blood sugar level	11  (46%)	10  (42%)	3  (13%)	10  (42%)	17  (71%)
Headache	3  (13%)	1  (4%)	1  (4%)	4  (17%)	5  (21%)

 = participants

	Group 3		
	Gliclazide tablet A medium release (out of 20 participants)	Gliclazide tablet B medium release (out of 20 participants)	Diamicron® MR (out of 20 participants)
Low blood sugar level	16  (80%)	5  (25%)	12  (60%)
Headache	3  (15%)	1  (5%)	1  (5%)
Gas	0 	1  (5%)	3  (15%)

 = participants

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What were the serious side effects?

A side effect is considered serious when:

- the participant needs to be hospitalised,
- it causes lasting damage or death,
- the participant's life is in danger or,
- it is medically important in the doctor's opinion.

In this study, no participants had serious side effects (serious unwanted medical events thought to be caused by the treatments in the study).

In the study, no participants died.

7 What were the study results?

The study was completed as planned.

This document presents only the results for the main goal of the study. Other results are available in other documents listed in Section 10.

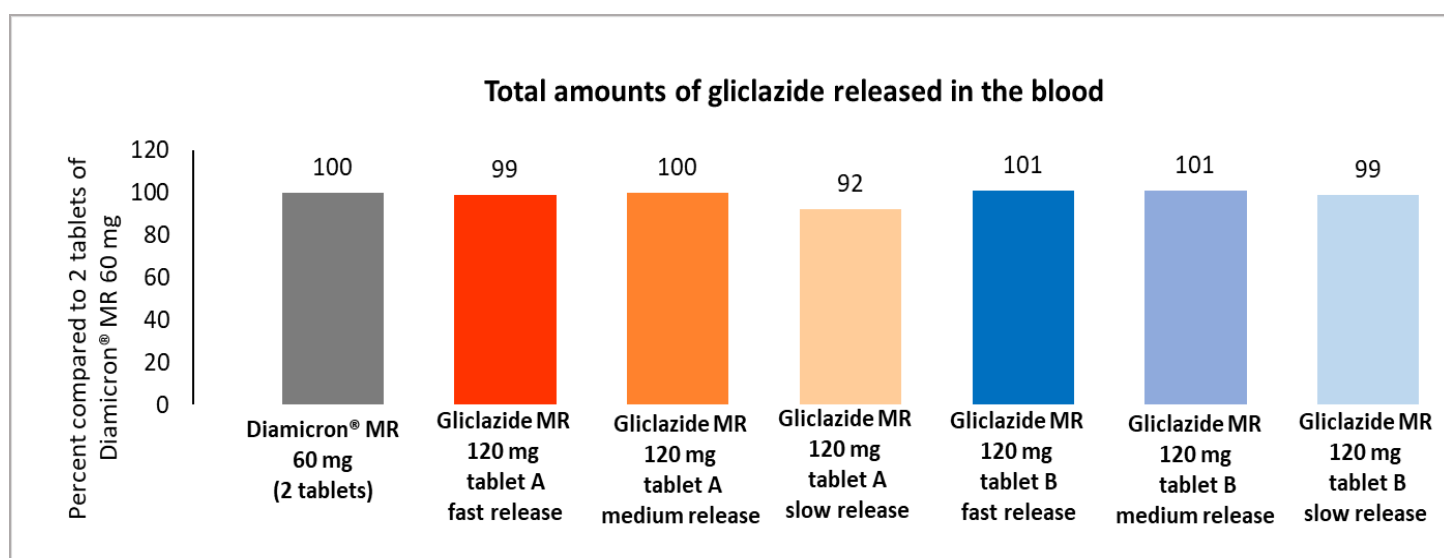
The researchers wanted to know how the 3 forms (fast, medium and slow release) of gliclazide MR 120 mg tablets A and B were absorbed into the body of healthy participants and moved through the blood, compared to 2 tablets of Diamicon® MR 60 mg.

To answer this question, the researchers measured the levels of gliclazide in the blood after participants received each treatment. In particular the researchers assessed:

- The total amount (maximum drug exposure) of gliclazide in the blood after receiving the study treatments.
- The highest level of gliclazide in the blood after receiving the study treatments.

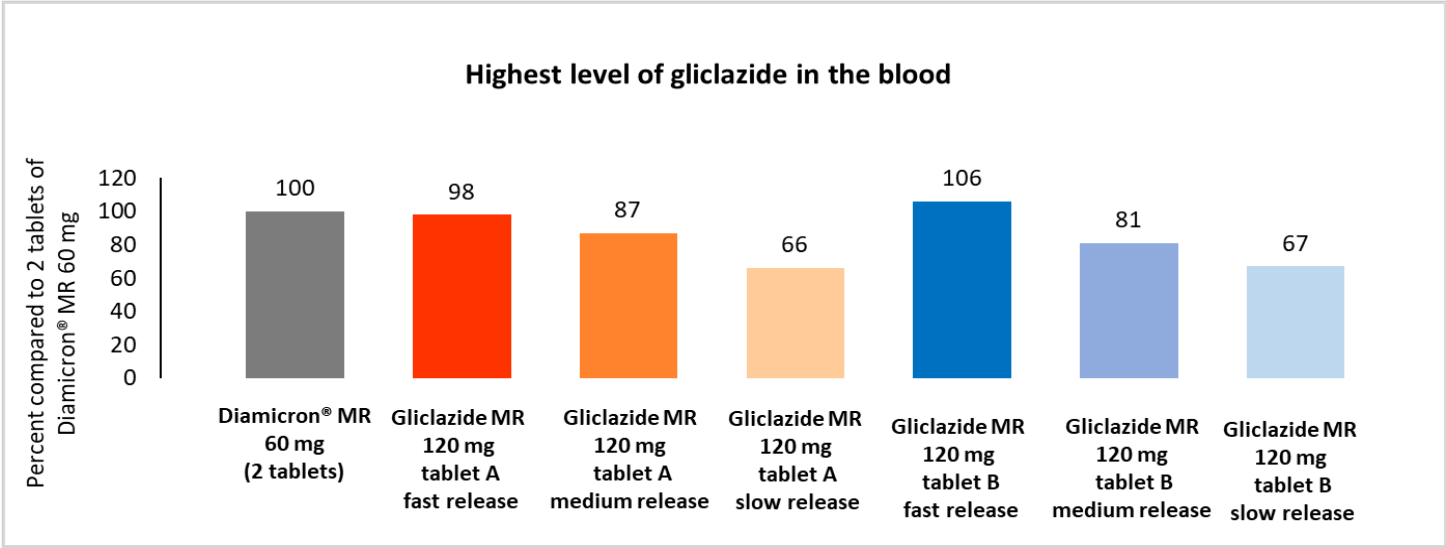
Group 1 and 2 (empty stomach):

Results for the total amounts of gliclazide in the blood and the highest level of gliclazide in the blood are shown below.



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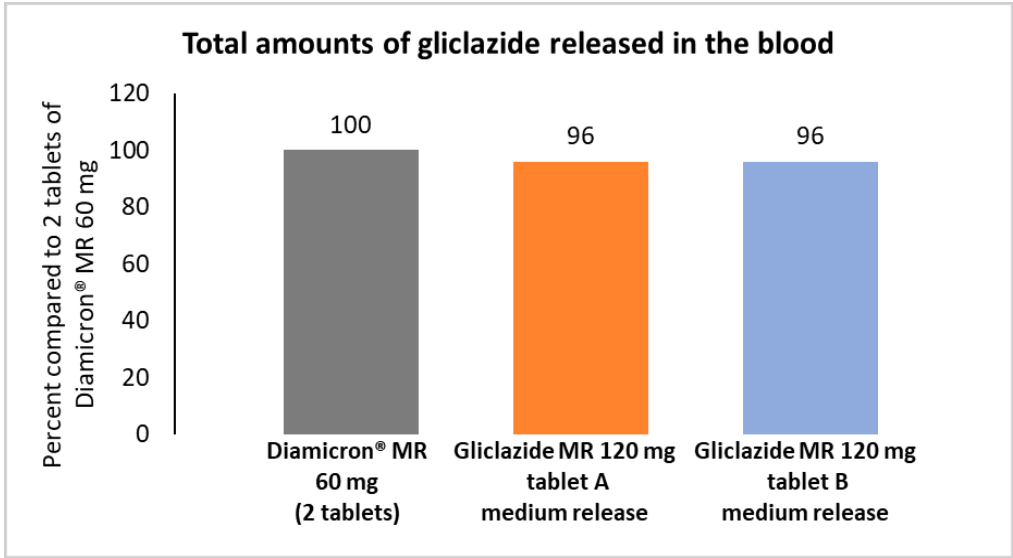


The total amounts and the highest level of gliclazide in the blood for the **fast release** form of gliclazide tablet **A** and **B** were similar to that of 2 Diamicon® MR 60 mg tablets.

For **medium** and **slow** release forms of tablets A and B, the total amounts of gliclazide released in the blood were also similar to that of 2 Diamicon® MR 60 mg tablets. However, the highest levels of gliclazide in the blood were lower than that of 2 Diamicon® MR 60 mg tablets and not within the acceptable range.

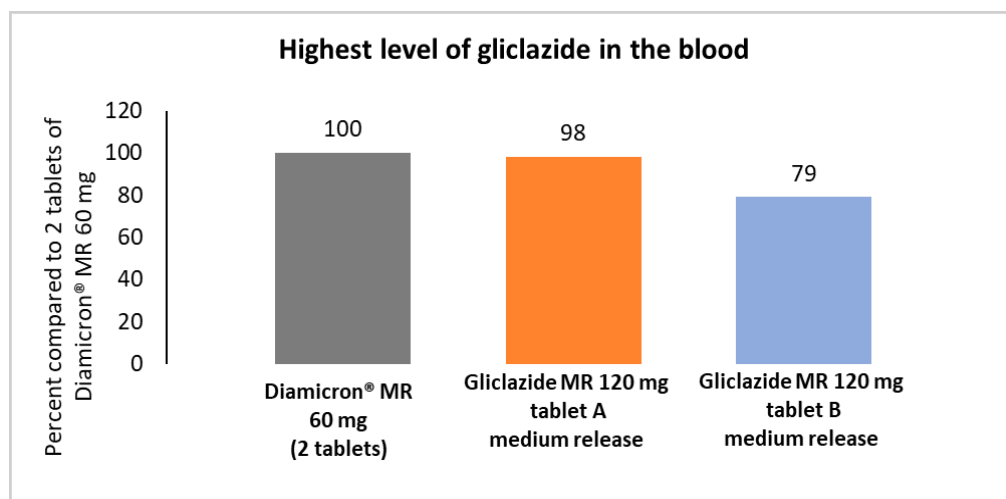
Group 3 (after eating a meal):

Results for the total amounts and the highest level of gliclazide released in the blood are shown below.



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For **medium release** form of gliclazide MR 120 mg tablet **A**, the total amounts of gliclazide in the blood as well as the highest level of gliclazide in the blood were similar to that of 2 Diamicron® MR 60 mg tablets.

For **medium release** form of gliclazide MR 120 mg tablet **B**, the total amounts of gliclazide released in the blood was also similar compared to 2 Diamicron® MR 60 mg. However, the highest level of gliclazide in the blood was lower than that of 2 Diamicron® MR 60 mg tablets and was not within the acceptable range.

8 How has this study helped research?

The researchers found that:

- The **fast release** form for the 2 formulations of gliclazide MR 120 mg tablets **A** and **B** showed similar bioavailability on an empty stomach compared to 2 Diamicron® MR 60 mg tablets.
- The **medium release** form of gliclazide MR 120 mg tablet **A** showed similar bioavailability after eating compared to 2 Diamicron® MR 60 mg tablets.

This study helped researchers learn more about how different forms of gliclazide MR 120 mg tablets A and B act in the body of healthy participants.

The results from this study in healthy adult participants will encourage interest and help guide future research to determine the appropriate type of gliclazide MR 120 mg tablets for treating patients who may need the highest dose of 120 mg.

This summary shows only the main results from this one study. Other studies, evaluating the same drug, may find different results.

9 Are there plans for further studies?

Further clinical studies with gliclazide are planned.

10 Further information

What are the identification numbers of the study?

- Protocol code: S005190-170
- EU Trial number: 2023-507802-15-00

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Who did the study?

The company that organised and funded the research, called the “sponsor”, is the Institut de Recherches Internationales Servier based in Gif-Sur-Yvette, France.

How can you contact the sponsor?

Contact us on the Servier website <https://servier.com/en/>.

Where can you learn more about this study?

You can find more information about this study on these websites:

- <https://euclinicaltrials.eu/>. Once you are on the website, type “2023-507802-15-00” into the search box and click “search”.
- <https://clinicaltrials.servier.com/find-clinical-trials>

In this document we translated medical terms into lay terms. You can find the corresponding medical terms in the Servier glossary at <https://clinicaltrials.servier.com/glossary/>

You can find general information about clinical trials on <https://clinicaltrials.servier.com/>