FOR IMMEDIATE RELEASE

HEALTH SCIENCES AUTHORITY
PRESS RELEASE
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HSA RECALLS THREE BRANDS OF LOSARTAN MEDICINES FROM HETERO LABS LTD

The Health Sciences Authority (HSA) is recalling three brands of blood pressure medicines, which contain a losartan ingredient that was manufactured by Hetero Labs Limited. These products were found to contain trace amounts of a nitrosamine impurity, N-nitroso-N-methyl-4-aminobutyric acid (NMBA), which are above internationally acceptable levels.

2. There is no immediate health risk associated with taking the affected medicines, and patients are advised not to stop treatment on their own. We have advised healthcare professionals to review the medicine and treatment plans of their patients.

3. Not all losartan medicines are affected by this recall. Only three out of the ten losartan products in Singapore contain unacceptable levels of nitrosamine impurity.

Table A: List of recalled losartan medicines

Product name	Active ingredient	Strength	Local supplier
Hyperten Tablet	Losartan Potassium	50mg	Goldplus Universal Pte Ltd
		100mg	
Losagen Tablet	Losartan Potassium	50mg	Medicell Pharmaceutical (S) Pte Ltd
		100mg	
Losartas Tablet	Losartan Potassium	50mg	Apotheca Marketing Pte Ltd
		100mg	

Please refer to **Annex A** for pictures of the medicine and its packaging.

4. Losartan belongs to a class of medicines called angiotensin II receptor blockers (ARBs), which are used to treat high blood pressure, also known as hypertension. In addition to the three recalled brands, there are seven other brands of losartan medicines marketed in Singapore. These seven brands have been tested by HSA and do not contain NMBA.

Background

5. Since June 2018, several ARB medicines have been recalled overseas due to the presence of two other nitrosamine impurities[1], Nitrosodimethylamine (NDMA) and N-Nitrosodiethylamine (NDEA). HSA had tested the locally marketed ARB medicines and none of them were found to contain unacceptable levels of the two impurities. The list of ARB medicine recalls and HSA's corresponding actions are below:

a) In end-June 2018, several valsartan-containing medicines were recalled overseas due to the presence of NDMA. Based on HSA's tests, none of valsartan products marketed in Singapore were affected.

b) In September 2018, several overseas regulatory agencies recalled affected ARBs due to the presence of NDEA. HSA had tested the ARBs marketed in Singapore and none were found to contain unacceptable levels of these impurities. Since November 2018, HSA has required companies to test for these impurities in their products and comply with international standards, to ensure the continued quality of the products imported into Singapore.

6. Since end-February 2019, several losartan medicines were recalled overseas due to the presence of NMBA. HSA has tested <u>all</u> locally marketed losartan products for the presence of the new NMBA impurity. By testing all brands of losartan medicines available locally beyond Hetero Labs products, HSA is able to advise which brands did not contain NMBA, and help healthcare professionals and patients decide on suitable alternatives in place of the recalled brands.

7. Tests and reviews were completed on 21 March 2019 and three brands – Losartas, Losagen and Hyperten – were found to contain trace amounts of NMBA that are above acceptable levels. The other seven brands of losartan products were not affected by this impurity. HSA is continuing to test all other ARB medicines marketed in Singapore to determine if they are affected by this impurity.

8. HSA is working with companies and international regulatory agencies to verify the cause of contamination, and to formulate measures to address the issue. HSA will require companies to make the necessary changes to their manufacturing process to ensure that the medicines do not contain these impurities in future.

Consumer Advisory

9. The risks of trace amounts of NMDA are associated with long term exposure. There is no immediate health risk to patients taking the affected products. Sudden

[1] Nitrosamines are environmental contaminants and they are also found in food or the environment in very minute amounts. Studies have reported that exposure over a prolonged period to doses of nitrosamine impurities (including NDMA, NDEA and NMBA) that are much higher than usual human exposure could cause cancer in animals. Exposure to nitrosamines at high quantities over a long-term period may potentially increase the risk of cancer. The trace amounts detected in the three recalled products are not expected to pose immediate harm to consumers.

stopping of the medicines can pose greater and more immediate risk to patient's health.

10. Professor Ding Zee Pin, Cardiologist in the National Heart Centre and HSA's Expert Panel on Nitrosamines advises: "There is no immediate health risk associated with taking the affected medicines, and patients are advised not to stop or change treatment on their own. As losartan is used to treat high blood pressure, stopping the medicine without replacements of other equivalent medication can increase the risk of poor control of blood pressure."

11. HSA advises consumers who are taking the three affected brands of losartan medicines on the following:

a) Do not stop taking the medicines on your own until you have been provided with a replacement brand of losartan or a different medicine by your healthcare provider.

b) Discuss your medication and treatment plan with your healthcare provider.

c) Only three of the ten losartan products in Singapore – Hyperten, Losagen and Losartas – contain the nitrosamine impurity. Consult your healthcare provider if you are unsure if you are taking an affected brand.

12. Consumers can contact the HSA hotline at Tel: 6866 1111 (Monday to Friday, 9am – 5pm) or email: hsa_info@hsa.gov.sg if you have further enquiries.

13. More details and updates on this issue of nitrosamine contamination of ARB medicines are posted on the HSA website at this link: https://www.hsa.gov.sg/sartanupdates

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About the Health Sciences Authority (HSA)

The Health Sciences Authority (HSA) applies medical, pharmaceutical and scientific expertise through its three professional groups, Health Products Regulation, Blood Services and Applied Sciences, to protect and advance national health and safety. HSA is a multidisciplinary authority. It serves as the national regulator for health products, ensuring they are wisely regulated to meet standards of safety, quality and efficacy. As the national blood service, it is responsible for providing a safe and adequate blood supply. It also applies specialised scientific, forensic, investigative and analytical capabilities in serving the administration of justice. For more details, visit http://www.hsa.gov.sg/.

For more updates on public health and safety matters, follow us on Twitter at www.twitter.com/HSAsg.

About HSA's Health Products Regulation Group

The Health Products Regulation Group (HPRG) of HSA ensures that drugs, innovative therapeutics, medical devices and health-related products are wisely regulated and meet appropriate safety, quality and efficacy standards. It contributes to the development of biomedical sciences in Singapore by administering a robust, scientific and responsive regulatory framework.

About Angiotensin II Receptor Blockers (ARBs)

ARB class of medicines is used for the control of high blood pressure and includes valsartan, losartan, candesartan, fimasartan, irbesartan and olmesartan.

About nitrosamine impurities

Nitrosamines are environmental contaminants and they are also found in food or the environment in very minute amounts. Studies have reported that exposure over a prolonged period to doses of nitrosamine impurities (including NDMA, NDEA and NMBA) that are much higher than usual human exposure could cause cancer in animals. Exposure to nitrosamines at high quantities over a long-term period may potentially increase the risk of cancer. The trace amounts detected in the three recalled products are not expected to pose immediate harm to consumers.