Advisory

Voluntary Recall of Irbesartan-containing Products:
Irbesartan (Aprovel) 150mg Film-Coated Tablet, Irbesartan (Aprovel) 300mg Film-Coated Tablet, Irbesartan + Amlodipine (Aprovasc) 150mg/5mg Film-Coated Tablet, Irbesartan + Amlodipine (Aprovasc) 300mg/5mg Film-Coated Tablet, Irbesartan + Amlodipine (Aprovasc) 300mg/10mg Film-Coated Tablet, Irbesartan + Hydrochlorothiazide (CoAprovel) 300mg/12.5mg Film-Coated Tablet

Taguig City, 04 March 2022

Sanofi, in agreement with the Philippine Food and Drug Administration, would like to inform you of the voluntary recall of several batches and a risk of market shortage for Irbesartan (Aprovel®), Irbesartan + Amlodipine (Aprovasc®) and Irbesartan + Hydrochlorothiazide (CoAprovel®).

Background on the voluntary recall

As per communication received from the European Directorate for the Quality of Medicines and Healthcare (EDQM) regarding potential mutagenic impurity (GTI) in irbesartan products, Sanofi, being one of the manufacturers of irbesartan products, voluntarily decided, on 10th Jun 2021, to put on hold the distribution of batches of medicines containing irbesartan (marketed worldwide under multiple trade names, including Aprovel®, Aprovasc® and CoAprovel®) where the level of GTI exceeds defined limit, or is unconfirmed. This decision followed the implementation of precautionary measures in November 2020 and Sanofi's decision to release only batches confirmed with impurity content below the defined limit, from January 2021.

In parallel, retrospective testing of unexpired marketed batches started in June 2021 and based on the results, Sanofi started recalling a limited number of batches that had been distributed in several countries. Early October 2021 all retrospective tests were completed. Most batches have been confirmed not to contain the impurity above the "less than lifetime" threshold defined by Sanofi in line with ICH M7 regulations and endorsed by the EMA and other Health Authorities. Sanofi has been liaising directly with any relevant Health Authorities since mid-October to propose the recall of any batches containing an impurity level above the "less than lifetime" threshold. In the Philippines, a voluntary recall of several batches was proposed by Sanofi as a precautionary measure to the Philippine Food and Drug Administration.

Patient safety is of the utmost importance to us. Sanofi is currently considering and taking all necessary actions that can help ensure the level of the GTI impurity is within the acceptable ICH M7 limits including releasing to the market batches with a content of GTI impurity is at or below ICH M7 acceptable limit since January 2021. As part of our remediation plan, Sanofi has established control limits for specific impurities found in finished irbesartan-containing drug products and amended manufacturing and quality assurance processes accordingly.

Sanofi performed a comprehensive assessment in December 2020 using global preclinical data, clinical data from the Sanofi pharmacovigilance (PV) database, PV textbooks, literature review. There are no data from the review with irbesartan-containing drug products to suggest that the product caused a change in the frequency or nature of reported adverse events of cancers, congenital

anomalies, or fertility disorders. Sanofi continues to closely monitor all malignancies through routine PV activities.

Affected batches and product information

Irbesartan (Aprovel) is indicated for the treatment of hypertension and the treatment of renal disease in patients with hypertension and type 2 diabetes.
Irbesartan + Amlodipine (Aprovasc) is indicated for the treatment of essential hypertension.
Irbesartan + Hydrochlorothiazide (CoAprovel) is indicated for the treatment of hypertension.

Below is the list of batches to be recalled:

Product Name	Dosage Strength	Registration No.	Batch No.	Expiry date
Irbesartan (Aprovel) Film-Coated Tablet	150mg	DRP-5716	AA271	Mar-23
			AA193	Apr-23
	300mg	DRP-5715	AA645	Apr-23
Irbesartan/ Amlodipine (Aprovasc) Film-Coated Tablet	150mg/5mg	DR-XY45509	AMXA006	Sep-23
			AMXA007	Sep-23
			AMXA008	Sep-23
			AMXA009	Sep-23
	300mg/5mg	DR-XY45507	AMXA003	Apr-23
	300mg/10mg	DR-XY45508	AMXA002	Jan-23
Irbesartan/ Hydrochlorothiazide (CoAprovel) Film-Coated Tablet	300mg/12.5mg	DRP-002	AA550	Aug-22

Instructions to the general public regarding the recall of the products

These medicines are used by many people to treat high blood pressure, or renal disease in patients with hypertension and type 2 diabetes (indications of each medicine specified above). The health risk of discontinuing these medicines without consulting a doctor or without an alternative treatment may be higher than the potential risk presented by the impurity. Patients should always consult their physicians if they have questions or concerns about their individual treatment. Medicines containing irbesartan can be bought only with a prescription and upon recommendation of a physician. All Sanofi products should be taken in accordance with leaflet instructions, which has been approved by local authorities. Patients and healthcare professionals have also the opportunity to contact the local Sanofi Medical Information helpline if needed at Medinfo.PH@sanofi.com and the Sanofi Quality Department at PH.QA@sanofi.com. Please note that no other batches of Irbesartan (Aprovel) 150mg and 300 mg Film-Coated Tablet, Irbesartan + Amlodipine (Aprovasc) 150mg/5mg, 300mg/5mg and 300mg/10mg Film-Coated Tablet, Irbesartan + Hydrochlorothiazide (CoAprovel) 300mg/12.5mg Film-Coated Tablet are included in this voluntary batch recall.

Contact for reporting

- Healthcare Professionals should report adverse reactions in accordance with the national spontaneous reporting system
- Adverse drug reactions must be reported to sanofi-aventis Philippines, Inc. at PV.Philippines@sanofi.com
- For suspected adverse drug reaction, you may also report to the FDA: www.fda.gov.ph or through https://primaryreporting.who-umc.org/Reporting/Reporter?OrganizationID=PH