IMPORTANT MEDICINE SAFETY INFORMATION

RECOMMENDED CALCULATIONS OF CONTRACEPTION DURATION AFTER COMPLETION OF THERAPY TO MINIMISE THE RISK OF EMBRYOTOXICITY AND TERATOGENICITY ASSOCIATED WITH THE USE OF GENOTOXIC ANTICANCER MEDICINES (INCLUDING POTENTIAL METABOLITES).

26 April 2024

Dear Healthcare Professional,

In collaboration with the South African Health Products Regulatory Authority (SAHPRA), the companies listed below would like to inform you about recommended calculations of contraception duration after completion of therapy with genotoxic anticancer medicines (including potential metabolites).

Background on the safety concern

The risk of genotoxic anticancer medicines (and their potential genotoxic metabolites) -mediated reproductive adverse events including, embryotoxicity and teratogenicity has been identified. In male patients, genotoxic anticancer medicines and their potential metabolites may cause DNA damage in the sperm, potentially resulting in adverse events in the embryo or foetus of a female sexual partner. In female patients, these products may directly affect the embryo or foetus; or may cause DNA damage in the oocytes.

To minimise the risk of drug-induced heritable DNA damage and to ensure that genomic integrity of gametes at the time of conception is maintained, patients are generally advised to use highly effective contraception during treatment and for an adequate period of time following the end of treatment with genotoxic medicines.

The Professional Information (PI) and Patient Information Leaflet (PIL) of genotoxic anticancer medicines listed below are or will be updated to appropriately reflect the revised safety information.

Advice to healthcare professionals

- Female patients and female sexual partners of male patients receiving genotoxic anticancer medicines, should be advised to use highly effective contraception, until the end of relevant systemic exposure to the genotoxic compound including potential genotoxic metabolites (i.e. five half-lives after the last dose) plus 6 months (equivalent to one folliculogenesis cycle).

- Female patients and female sexual partners of male patients receiving pure aneugenic pharmaceuticals, should be advised to use highly effective contraception, until the end of relevant systemic exposure to the products (i.e. five half-lives after the last dose) plus 1 month. It should be noted that only dividing oocytes are affected by aneugenicity.

- Male patients should be advised to use highly effective contraception, until the end of relevant systemic exposure to the pure aneugenic or genotoxic compound including potential genotoxic metabolites (i.e. five half-lives after the last dose) plus 90 days (equivalent to one sperm cycle).

- Healthcare professionals are urged to report any adverse drug reactions (ADRs) or product quality problems associated with the use of the products listed below to the relevant companies indicated in the table below, or to SAHPRA via the eReporting link: https://primaryreporting.who-umc.org/ZA available on the SAHPRA website (www.sahpra.org.za).

- Alternatively, please complete the ADR reporting form accessible via the SAHPRA website at https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/ and email it to adr@sahpra.org.za .

- Additionally, reporting can be done via the Med Safety App. The App can be downloaded into a smart mobile phone through Google Play or App Store. For more information on Med Safety App, please visit https://medsafety.sahpra.org.za/.

- For more information on ADR reporting of products listed below, please contact the SAHPRA Pharmacovigilance unit at pvqueries@sahpra.org.za or alternatively use the contact details indicated below.

- For product specific information regarding the half-life, as well as recommendations regarding duration for use of contraception after completion of genotoxic anticancer therapy, please contact the company responsible for the product/s listed below.

Company contact points

COMPANY	PRODUCT	ACTIVE INGREDIENT	REG NO	Contact details
sanofi-aventis south africa (pty) ltd	OXALIWIN 50 mg/10 mL RTU	Oxaliplatin 50 mg/10 mL	A39/26/0521	ZA.DrugSafety@sanofi.com ZA.Medinfo@sanofi.com
	OXALIWIN 100 mg/20 mL RTU	Oxaliplatin 100 mg/20 mL	A39/26/0522	
	DOCETERE 20 MG/1 ML RTU	Docetaxel 20 mg/1 mL	44/26/0098	
	DOCETERE 80 MG/4 ML RTU	Docetaxel 80 mg/4 mL	44/26/0099	
Key Oncologics (Pty) Ltd	Abraxane	Albumin bound paclitaxel	50/26/0182	Jean Lambrechts Responsible Pharmacist Tel : 011 483 0060/5 084 562 0292 Email : jean@keyoncologics.co.za Mari Nicolaides Pharmacovigilance Manager Tel : 011 483 0060/5 071 689 9131 Email : mari@keyoncologics.co.za
	Biolyse Paclitaxel 30mg	Paclitaxel	36/26/0024	
	Cosmegen 0,5mg	Dactinomycin	54/26/0380	
	Dacin 200*	Dacarbazine	47/26/0837	
	Doxopeg 20mg	Liposomal doxorubicin hydrochloride	A40/26/0389	
	Key Docetaxel 20mg	Docetaxel	45/26/0328	
	Key Docetaxel 80mg	Docetaxel	45/26/0329	
	Navelbine Oral 20mg	Vinorelbine	36/36/0012	
	Navelbine Oral 30mg	Vinorelbine	36/26/0013	
	Oxaliplatin Key 50	Oxaliplatin	45/26/0030	
	Oxaliplatin Key 100	Oxaliplatin	45/26/0031	
	Phenasen	Arsenic Trioxide	52/26/0019	
	Vidaza	Azacitidine	A40/26/0521	
	Yondelis 1mg	Trabectidin	43/26/0557	
AstraZeneca Pharmaceuticals (Pty) Ltd	Lynparza 100	Olaparib 100 mg	52/26/0745	SA.MEAMedInfo@astrazeneca.com
	Lynparza 150	Olaparib 150 mg	52/26/0746	
Pfizer Laboratories (PTY) Ltd	Xalkori 200mg	Crizotinib 200 mg	47/26/0568	ZAF.AEReporting@pfizer.com https://www.pmiform.com/HCP/SSAF
	Xalkori 250mg	Crizotinib 250mg	47/26/0569	
	Inlyta 1mg	Axitinib 1mg	48/26/0605	
	Inlyta 3mg	Axitinib 3mg	48/26/0606	
	Inlyta 5mg	Axitinib 5mg	48/26/0607	
	Inlyta 7mg	Axitinib 7mg	48/26/0608	
	Palbociclib Pfizer 75mg	Palbociclib 75mg	52/26/0041	
	Palbociclib Pfizer 100mg	Palbociclib 100mg	52/26/0042	
	Palbociclib Pfizer 125mg	Palbociclib 125mg	52/26/0043	
	Sutent 12,5mg Capsules	Sunitinib malate 12,5mg	41/26/0197	
	Sutent 25mg Capsules	Sunitinib malate 25mg	41/26/0195	
	Sutent 50mg Capsules	Sunitinib malate 50mg	41/26/0196	
	Kessar 20	Tamoxifen citrate 20mg	S/21.12/359	
Janssen Pharmaceutica (PTY) LTD	Velcade 1mg	Bortezomib 1,0 mg	43/26/0427	AdverseEventZA@its.jnj.com
	Velcade	Bortezomib 3,5 mg	A40/26/0005	
	Dacogen	Decitabine 1x 50mg vial	46/26/0608	
Bayer (Pty) Ltd	Nexavar 200	Sorafenib	A40/26/0776	pv.sewa@bayer.com za-medinfo@bayer.com

*The recommendations for this product may not align with the recommendations above. Please contact the relevant company for further information

References

1. U.S. Department of Health and Human Services; Food and Drug Administration; Center for Drug Evaluation and Research (2019) Oncology Pharmaceuticals: Reproductive Toxicity Testing and Labeling Recommendations. Guidance for Industry. Office of Communications, Food and Drug Administration, Silver Spring, MD, USA

2. European Medicines Agency (2023) SWP/NcWP recommendations on the duration of contraception following the end of treatment with a genotoxic drug European Medicines Agency, Amsterdam, The Netherlands; EMA/CHMP/SWP/74077/2020 rev. 1*

3. Heads of Medicines Agencies, Clinical Trials Facilitation and Coordination Group (2020) Recommendations related to contraception and pregnancy testing in clinical trials. Accessible at https://www.hma.eu/fileadmin/dateien/Human_Medicines/01-About_HMA/Working_Groups/CTFG/2020_09_HMA_CTFG_Contraception_guidance_Version_1.1.pdf

Yours Sincerely,

Yusuf Dawood *Local Pharmacovigilance Officer – South Africa* *Country Safety Head – South Africa* **sanofi-aventis south africa (pty) ltd** Signature: *Electronically signed by: YUSUF DAWOOD Reason: Approval Date: Apr 26, 2024 16:06 GMT+2*	Jean Lambrechts *Responsible Pharmacist* **Key Oncologics (Pty) Ltd** Signature: *Electronically signed by: JJ Lambrechts Reason: Final signoff Date: Apr 26, 2024 15:36 GMT+2*	Malini Liese *Senior Regulatory affairs Manager and Responsible Pharmacist* **AstraZeneca Pharmaceuticals (Pty) Ltd** Signature: *Electronically signed by: Malini Liese Reason: approved Date: Apr 26, 2024 16:59 GMT+2*
Lawrene Makamu *Country Safety Lead* **Pfizer Laboratories (PTY) Ltd** Signature: *Electronically signed by: Lawrene Makamu Reason: I approve this document. Date: Apr 26, 2024 15:12 GMT+2*	Vanessa Snow *Head of Medical Affairs* **Janssen Pharmaceutica (Pty) Ltd** Signature: *Electronically signed by: Vanessa Snow Reason: Approval and acknowledgment on behalf of Janssen Pharmaceutica Date: Apr 26, 2024 14:54 GMT+2*	Shadika Baijnath *Head of Commercial Quality & Responsible Pharmacist* **Janssen Pharmaceutica (Pty) Ltd** Signature *Electronically signed by: Shadika Baijnath Reason: Approval Date: Apr 26, 2024 15:41 GMT+2*
Dr. Thuli Makhene *Pharmacovigilance Country Head* **Bayer (Pty) Ltd** Signature: *Electronically signed by: Thuli Makhene Reason: Reviewed Date: Apr 26, 2024 14:57 GMT+2*		