

IMPORTANT MEDICINE SAFETY INFORMATION

RECOMMENDED CALCULATION OF CONTRACEPTION DURATION AFTER COMPLETION OF THERAPY TO MINIMISE THE RISK OF GENOTOXIC ANTICANCER MEDICINE-MEDIATED REPRODUCTIVE ADVERSE EVENTS

13 June 2024

Dear Healthcare Professional,

In collaboration with the South African Health Products Regulatory Authority (SAHPRA), Dr. Reddy's Laboratories (Pty) Ltd would like to draw your attention to the recommended calculations of contraception duration after completion of therapy with genotoxic anticancer medicines (including potential genotoxic metabolites).

Summary

- The risk of genotoxic anticancer medicines (and their potential genotoxic metabolites) – mediated reproductive adverse events including, embryotoxicity and teratogenicity has been identified.
- To minimise embryofoetal developmental risk while receiving and after completion of therapy with genotoxic anticancer medicines, new calculations for contraception is recommended in female patients receiving the genotoxic anticancer medicines and to female sexual partners of male patients receiving the genotoxic pharmaceuticals.

Background on the safety concern

Due to their genotoxic nature, anti-cancer therapies may cause spontaneous abortions, infertility or heritable damage to the offspring and possibly to the subsequent generations. In males, genotoxic products may cause DNA damage in the sperm, potentially resulting in adverse events in the embryo or foetus of a female sexual partner. In females, genotoxic 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 will be updated to appropriately reflect the revised calculations of contraception duration after completion of therapy with these medicines (including potential genotoxic metabolites).

Advice to Healthcare professionals

- Male patients 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 90 days (i.e., 60-75 days for sperm production plus 10-14 days for the transport to epididymis).

- 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 (which covers the growth and maturation phase of folliculogenesis).
- 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 Dr. Reddy's, or to SAHPRA by completing an ADR reporting form accessible via the SAHPRA website at <https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problemreporting-form/> and sending it to adr@sahpra.org.za.
- Alternatively, healthcare professionals may use eReporting link: <https://primaryreporting.who-umc.org/ZA> available on the SAHPRA website (www.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:

Company	Product name	Active ingredient	Registration Number	Contact details
Dr Reddy's Laboratories (Pty) Ltd	Azacitidine DRL	Azacitidine	51/26/0144	Herman Beyers Responsible Pharmacist Tel: +27 11 324 2100 AdverseEvents.SA@drreddys.com
	Bertred 1	Bortezomib	55/26/0005	
	Bertred 3,5	Bortezomib	51/26/0714	
	Riqviva 100	Bevacizumab	56/26/0604	
	Riqviva 400	Bevacizumab	56/26/0605	
	Redditux 100	Rituximab	56/26/0286	
	Redditux 500	Rituximab	56/26/0287	
	Sopilcin 20	Doxorubicin	51/26/0265	
	Sopilcin 50	Doxorubicin	51/26/0266	
	Eranfu 250	Fulvestrant	51/21.12/0740	

Dr Reddy's Laboratories (Pty) Ltd.				Herman Beyers Responsible Pharmacist Tel: +27 11 324 2100 AdverseEvents.SA@drreddys.com
	Suzopa 12,5	Sunitinib	56/26/0289	
	Suzopa 25	Sunitinib	56/26/0290	
	Suzopa 50	Sunitinib	56/26/0291	
	Lenalidomide DRL 5	Lenalidomide	52/26/0791	
	Lenalidomide DRL 10	Lenalidomide	52/26/0792	
	Lenalidomide DRL 15	Lenalidomide	52/26/0793	
	Lenalidomide DRL 25	Lenalidomide	52/26/0794	
	Teronred 250	Abiraterone	51/21.12/0732	
	Teronred 500	Abiraterone	56/21.12/0715	
	Abiraterone DRL 250	Abiraterone	50/21.12/0857	
	Egrotib 25	Erlotinib	56/26/0128	
	Egrotib 100	Erlotinib	56/26/0129	
	Egrotib 150	Erlotinib	56/26/0130	
	Bendamustine 180 mg / 4 ml DRL	Bendamustine	56/26/0216	
	Tazatred 20	Dasatinib	55/26/0797	
	Tazatred 50	Dasatinib	55/26/0798	
	Tazatred 70	Dasatinib	55/26/0799	
Tazatred 100	Dasatinib	55/26/0800		

Yours sincerely,

DocuSigned by:
Herman Beyers
Signer Name: Herman Beyers
Signing Reason: I approve this document
Signing Time: 15-Jun-24 | 1:56:08 AM IST
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Herman Beyers

Responsible Pharmacist

Dr Reddy's Laboratories (Pty) Ltd

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. Suzuki, N., Takai, Y., Yonemura, M. et al. Guidance on the need for contraception related to use of pharmaceuticals: the Japan Agency for Medical Research and Development Study Group for providing information on the proper use of pharmaceuticals in patients with reproductive potential. *Int J Clin Oncol* 27, 829–839 (2022). <https://doi.org/10.1007/s10147-022-02149-1>
4. Banholzer ML, Wandel C, Barrow P, Mannino M, Schmitt G, Guérard M, Müller L, Greig G, Amemiya K, Peck R, Singer T and Doessegger L. Clinical trial considerations on male contraception and collection of pregnancy information from female partner: update. *Clin Trans Med* 5:23, 2016. <https://doi.org/10.1186/s40169-016-0103-8>.