Identifying carcinogenic hazards among pharmaceutical agents: an update from the *IARC Monographs* Programme

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Cancer hazard from pharmaceutical exposure is a concern for patients and workers producing or handling pharmaceuticals.

Which pharmaceuticals are classified as human carcinogens by the *IARC Monographs* programme?

65 pharmaceuticals evaluated (1971-2023): 21 ***carcinogenic*** (IARC Group 1), 11 ***probably carcinogenic*** (Group 2A), 33 ***possibly carcinogenic*** (Group 2B) (Figure 1).

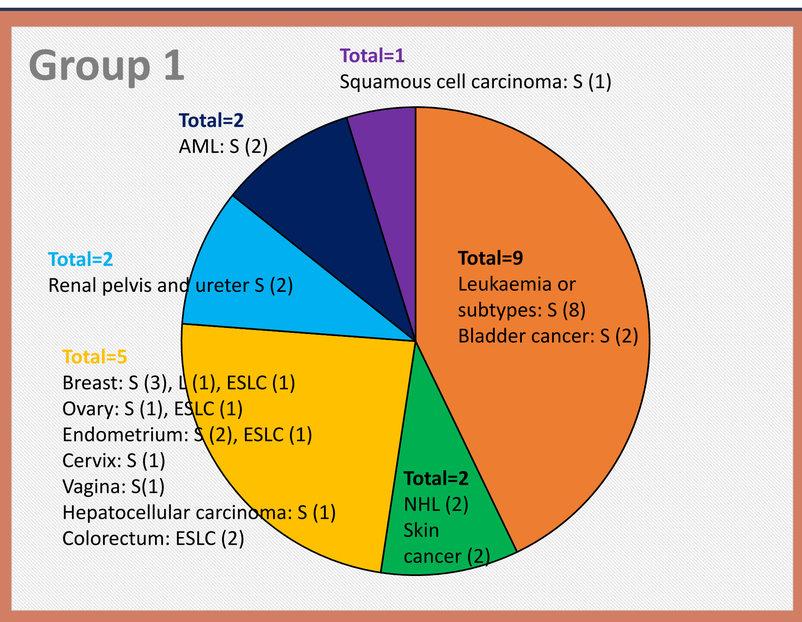
All Group 1 antineoplastics chemotherapeutics have evidence of treatment-related leukaemia, except chlornaphazine with blader cancer evidence only (Table 1, Figure 1).

Group 1 anti-neoplastic agents exhibited evidence of genotoxicity, hormonal pharmaceuticals also for modulation of receptor-mediated effect. Immunosuppression explained lymphomas caused by immunosuppressants (Table 1).

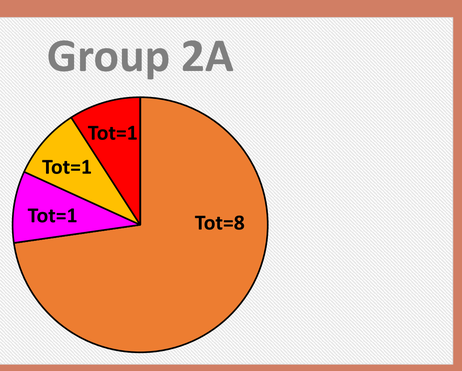
Table 1: Cancer in humans and mechanistic evidence for *IARC Monographs* Group 1 pharmaceuticals

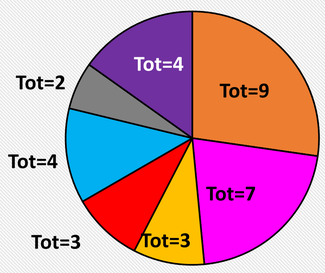
	Cancer sites with *sufficient*, *limited*, or *ESLC* evidence in humans	Mechanistic evidence
Anti-neoplastic		
MOPP (mechlorethamine, vincristine, procarbazine and prednisone)	Acute myeloid leukaemia, lung	Genotoxicity
Etoposide in combination with cisplatin and bleomycin	Acute myeloid leukaemia	Genotoxicity
Melphalan	Acute myeloid leukaemia	Genotoxicity
Semustine	Acute myeloid leukaemia	Genotoxicity
Chlorambucil	Acute myeloid leukaemia	Genotoxicity
Chlornaphazine	Bladder cancer	Genotoxicity
Cyclophosphamide	Acute myeloid leukaemia, bladder cancer	Genotoxicity
Treosulfan	Acute myeloid leukaemia	Genotoxicity
Busulfan	Acute myeloid leukaemia	Genotoxicity
Thiotepa	Leukaemia (all combined)	Genotoxicity
Etoposide	Limited evidence in humans, final determination is Group 1 on basis of observation of chromosomal translocation affecting MLL gene for treatment related leukaemia	Genotoxicity
Immunosuppressant		
Azathioprine	Skin (Squamous cell carcinoma), NHL	Genotoxicity, Immunosuppressive
Cyclosporine	Skin (Squamous cells carcinoma), NHL, multiple sites (unspecified)	Genotoxicity, Immunosuppressive
Hormonal agents		
Oestrogen only menopausal therapy	Sufficient: endometrium, ovary Limited: breast	Genotoxicity, modulation of receptor mediated- effect,
Oestrogen-progestogen menopausal therapy (combined)	Sufficient: breast, endometrium	Genotoxicity, Modulation of receptor mediated-effect
Oestrogen-progestogen oral contraceptives (combined)	Sufficient: breast, liver, uterine cervix Evidence suggesting lack of carcinogenicity (ESLC): ovary, endometrium	Genotoxicity, Modulation of receptor mediated- effect
Diethylstilbesterol	Sufficient: breast, vagina, uterine cervix Limited: endometrium, testis	Genotoxicity, Modulation of receptor mediated- effect; Contributory factors: Altered cell proliferation, epigenetic
Tamoxifen	Sufficient: endometrium ESLC: breast	Genotoxicity, Receptor mediated effect
Other drugs		
Methoxsalen plus UVA radiation	Skin (squamous cell carcinoma)	Genotoxic mechanism that involves photo-activation
Phenacetin and Phenacetin, analgesic mixture containing phenacetin	Renal pelvis and ureter	Genotoxicity

Figure 1: Group 1, 2A, and 2B pharmaceuticals grouped by class. For Group 1 agents, cancer types with *sufficient*, *limited*, or *ESLC* evidence are also listed.



Legend
Antineoplastic
Immunosuppressant
Antibiotics, antivirals, antifungal
Hormonal
Diabetic/cardiovascular
Analgesic/Antipsychotic
Implants
Anticancer chemotherapy regimen
Other





AML, Acute myeloid leukaemia; Tot, Total number of pharmaceuticals, S, Sufficient, L, Limited; ESLC, Evidence suggesting lack of carcinogenicity; in parenthesis number of pharmaceuticals per cancer type/determination.

Which pharmaceuticals are recommended for evaluation for the 2025-2029 period?

29 pharmaceuticals or treatment regimens submitted for reviewed and evaluated by the advisory group.
22 pharmaceuticals recommended high priority for evaluation, including antineoplastics (8), hormonal (4), and immunosuppressor agents (2) (Table 2)

Table 2: Pharmaceuticals with high priority for evaluation (2025-2029)

Evidence streams	
Relevant human cancer, animal cancer, and mechanistic evidence	**Antineoplastic**: Platinum-based chemotherapies as mechanistic class¶; Daunorubicin; Doxorubicin; **Hormonal**: GLP-1 analogues*; Clomiphene citrate*; Progestogen-only contraceptives* **Immunosuppressant**: Methotrexate **Analgesics**: Paracetamol/acetaminophen **Implants**: Textured implants (breast and buttock)
Relevant human cancer and mechanistic evidence	**Antineoplastic**: Anthracyclines as mechanistic class¶; BRAF inhibitors (Dabrafenib, Encorafenib, Vemurafenib); Epirubicin **Immunosuppressant**: Tofacitinib and other Janus kinase inhibitors **Anti-infection**: Tetracycline **Therapies combination**: Assisted reproductive techniques
Relevant mechanistic evidence	Anaesthetics, antipsychotic: Methamphetamine; Anaesthetics, volatile-isoflurane, sevoflurane, and desflurane
Group 1 carcinogen with evidence for new cancer sites	Hormone replacement therapy*

*Advised to conduct in latter half of 5-year period; ¶Advised to evaluate each pharmaceutical individually in the same volume; Agents never been evaluated by the IARC Monograph programme are underlined

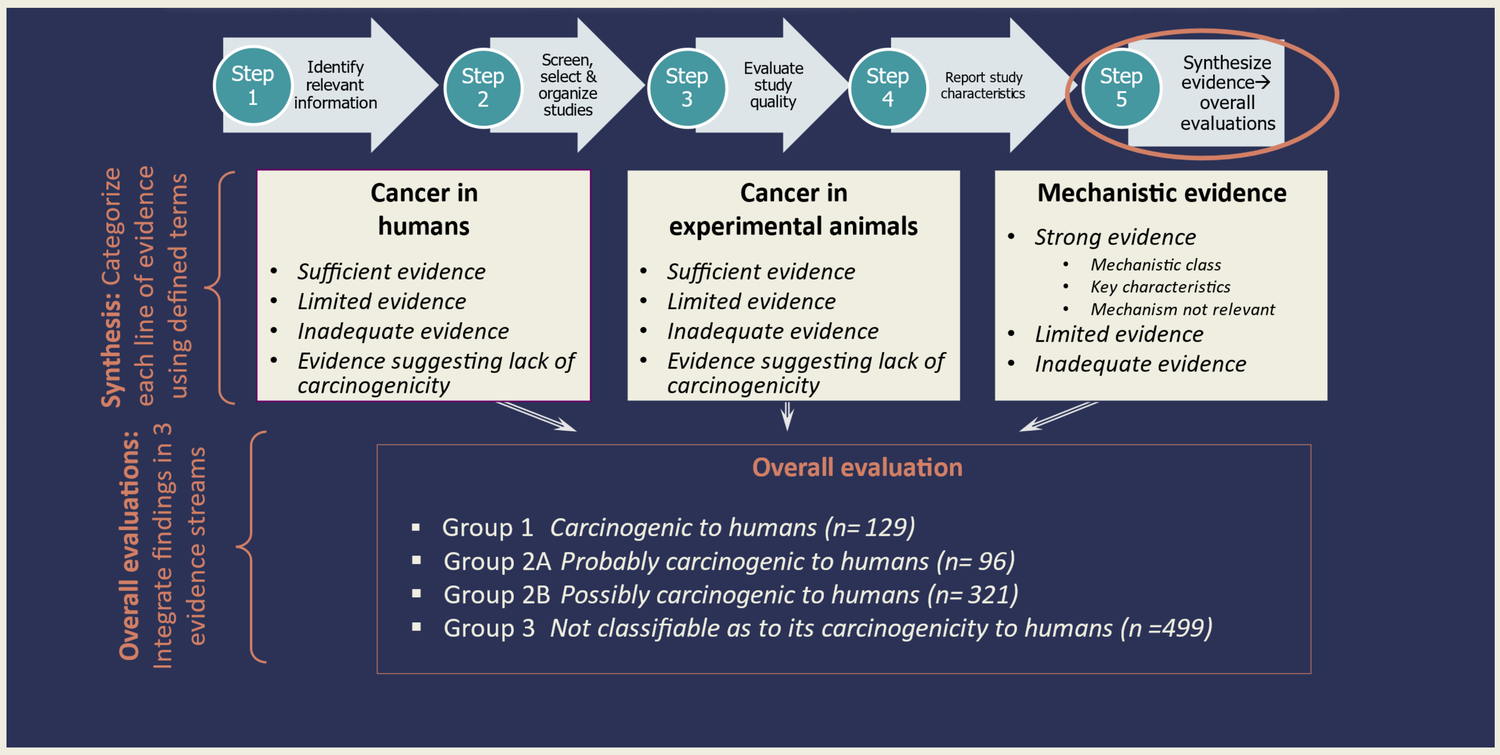
How IARC Monographs evaluations are conducted:

Useful links:

List of carcinogens classified by *IARC Monographs*
https://monographs.iarc.who.int/list-of-classifications

Download publications from the *IARC Monographs* programme
https://monographs.iarc.who.int/cards_page/publications-monographs/

Read and subscribe to *IARC Monographs* newsletter
https://monographs.iarc.who.int/iarc-monographs-news-3/



International Agency for Research on Cancer

World Health Organization

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