Disorders of purine and pyrimidine metabolism

CHI Formulary Treatment algorithm

Treatment algorithm-January 2024

Supporting treatment algorithms for the clinical management of disorders of purine and pyrimidine metabolism

Figure 1 outlines a comprehensive treatment algorithm on **the management of disorders of purine and pyrimidine metabolism** aimed at addressing the different lines of treatment after thorough review of medical and economic evidence by CHI committees.

For further evidence, please refer to CHI **Disorders of purine and pyrimidine metabolism** full report. You can stay updated on the upcoming changes to our formulary by visiting our website at https://chi.gov.sa/AboutCCHI/CCHIprograms/Pages/IDF.aspx

Our treatment algorithm offers a robust framework for enhancing patient care and optimizing treatment outcomes across a range of treatment options, holding great promise for improving healthcare delivery.

Treatable inborn errors of P/P metabolism.

Disease group	P/P defects	Treatment	Outcomes
Severe combined immunodeficiency (SCID)	• Adenosine deaminase deficiency (ADA deficiency) • Purine nucleoside phosphorylase deficiency (PNP deficiency)	• ERT with PEG-ADA • allogenic HSCT • autologous GT	• ERT with PEG-ADA: improves endogenous immune function and helps in recovery from infections, however only suboptimal immune reconstitution • HSCT: better overall survival • GT: reduced rate of infections, robust immune reconstitution
Disorders associated with overexcretion of insoluble purines and nephrological consequences	Uric acid: • Hypoxanthine-guanine phosphoribosyltransferase (HPRT) deficiency complete & partial • Phosphoribosylpyrophosphate synthase (PRPS) superactivity 2,8-dihydroxyadenine: • Adenine phosphoribosyltransferase (APRT) deficiency (2,8-diOH-adeninuria) Xanthine: • Xanthine dehydrogenase (XDH) deficiency (xanthinuria-I)	• XOR inhibitors (*e.g.*, allopurinol) • high-fluid intake • alkalization of the urine by administration of bicarbonate or citrate (not successful in APRT deficiency) • low-purine diet	• prevention of renal failure from crystal nephropathy • improvement of renal function
Disorders associated with hematological manifestations	Uridine monophosphate synthase (UMPS) deficiency (orotic aciduria)	• supplementation with uridine	• induces prompt hematological response and acceleration of growth • does not prevent suboptimal physical and mental development
Pharmacogenetic syndromes	• Dihydropyrimidinase (DHP) deficiency (dihydropyrimidinuria) • Dihydropyrimidine dehydrogenase (DPD) deficiency (thymine-uraciluria) • Ureidopropionase (UP) deficiency (NC-BALA amidohydrolase deficiency, ureidopropionic aciduria) • Thiopurine methyltransferase (TPMT) deficiency	• withdrawal of offending drug • dose adjustment	• prevention of pharmacogenetic syndrome
Other	• CAD deficiency	• uridine supplementation	• immediate cessation of seizures • resolution of anisopoikylocytosis • improved development
	• TP deficiency (MNGIE)	• HSCT • OLT	• effective in permanently restoring the biochemical imbalance • risk for complications and mortality related to HSCT • metabolic complications chronic kidney insufficiency, diabetes or cardiovascular disease related to life-long immunosuppressive therapy

ERT: enzyme replacement therapy; GT: gene therapy; HSCT: hematopoietic stem cell transplant; OLT: orthotopic liver transplantation; PEG-ADA: polyethylene glycol-conjugated adenosine deaminase; XOR: xanthine oxidoreductase.

Figure 1: Summary table of treatable purine and pyrimidine metabolism disorders