

**The Hospital for Sick Children
Technology Assessment at SickKids (TASK)**

APPENDICES

**THIOPURINE S-METHYLTRANSFERASE TESTING FOR AVERTING
DRUG TOXICITY IN PATIENTS RECEIVING THIOPURINES: A
SYSTEMATIC REVIEW AND QUALITY APPRAISAL**

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose.

Appendix A – Search strategies

BIOSIS

Set	Results	
# 10	<u>820</u>	#9 AND #8 Indexes=BIOSIS Previews Timespan=All years
# 9	<u>4,439,958</u>	#6 OR #5 Indexes=BIOSIS Previews Timespan=All years
# 8	<u>1,162</u>	#7 AND #4 Indexes=BIOSIS Previews Timespan=All years
# 7	<u>39,322</u>	#3 OR #2 OR #1 Indexes=BIOSIS Previews Timespan=All years
# 6	<u>3,876,558</u>	TOPIC: ("pharmacogenetics" or "genetics" or "genetic testing" or "heterozygote detection" or "genotype" or "sequence analysis" or "heterozygote" or "homozygote" or "hemizygote" or "genetic techniques" or "genetic association studies" or "genome-wide association study" or "genetic testing" or "genotyping techniques" or "restriction mapping" or "restriction fragment length polymorphism" or "single-stranded conformational polymorphism" or "oligonucleotide array sequence analysis" or "polymerase chain reaction" or "pharmacological biomarkers" or "genetic markers" or "biological markers" or "genetic predisposition to disease" or "amplification refractory mutation system" or "microchip" or "pharmacogen*" or "toxicogen*" or "(genotyp* or genetic*) (test or tested or tests or testing or predispos* or screen*)" or "biomarker*" or "PCR") Indexes=BIOSIS Previews Timespan=All years
# 5	<u>847,527</u>	TOPIC: ("phenotype" or "high pressure liquid chromatography" or "hplc" or "clinical laboratory techniques" or "clinical chemistry tests" or "cytological techniques" or "hematologic tests" or "radioligand assay" or "analytical chemistry techniques" or "enzyme assays" or "clinical enzyme tests" or "mass spectrometry" or "tandem mass spectrometry" or "chromatography" or "liquid chromatography" or "cytologic* techniq*" or "cytologic* technic*" or "hematolog* (test or tests or testing)" or "(haematolog* (test or tests or testing)" or "blood (test or tests or testing)" or "radioassay*" or "radioreceptor*" or "radioligand*") Indexes=BIOSIS Previews Timespan=All years
# 4	<u>5,467</u>	TOPIC: ("methyltransferases" or "thiopurine methyltransferase*" or "thiopurine s methyltransferase*" or "e.c. 2.1.1.67" or "tpmt") Indexes=BIOSIS Previews Timespan=All years

# 3	<u>5,996</u>	<p>TOPIC: ("6-mercaptopurine" or "6 mercaptopurine" or "6 mercapto purine" or "6 mercaptopurin" or "6 mercaptopurin monohydrate" or "mercaptopurin*" or "thiopurine*" or "6-thiopurine" or "leupurin*" or "bw 57323h" or "6 thiohypoxanthine" or "6-thiohypoxanthine" or "monohydrate puri-nethol" or "bw 57 323h" or "puri nethol" or "purimethol" or "purinethol" or "bw 57-323h" or "17-dihydro-6h-purine-6-thione mercaptopurine" or "6 mp" or "6 purinethiol" or "6 purinethiol hydrate" or "classen" or "empurine" or "ismipur" or "leukerin" or "loulla" or "mercaleukin" or "mercapurene" or "mern" or "mycaptine" or "nsc 755" or "nsc755" or "purine 6 thiol" or "purine thiol (6)" or "purinethiol" or "thiohypoxanthine" or "xaluprine")</p>
Indexes=BIOSIS Previews Timespan=All years		
# 2	<u>5,217</u>	<p>TOPIC: ("thiopurine*" or "thioguanin*" or "tioguan*" or "2 amino 6 purinethiol" or "tabloid" or "6 thioguanin*" or "lanvis" or "2 amino 6 mercaptopurine" or "2 amino purine 6 thiol" or "2 aminopurine 6 thiol" or "6 mercaptoguanine" or "6 thioquanine" or "nsc 752" or "nsc752" or "thioguanidine")</p>
Indexes=BIOSIS Previews Timespan=All years		
# 1	<u>33,633</u>	<p>TOPIC: ("azathioprine" OR "thiopurine*" OR "imurel" OR "immuran" OR "imuran" OR "6 (1 methyl 4 nitro 5 imidazolyl) mercaptopurine" OR "arathioprin*" OR "aza-q" OR "azafalk" OR "azahexal" OR "azamedac" OR "azamun*" OR "azanin" OR "azapin" OR "azapress" OR "azaprime" OR "azarex" OR "azasan" OR "azathiodura" OR "azathipine" OR "azathiopurine" OR "azathropsin" OR "azatioprina" OR "azatrox" OR "azatrilem" OR "azopi" OR "azoran" OR "azothioprin" OR "bw 57 322" OR "bw57322" OR "bw57-322" OR "bw 57322" OR "colinsan" OR "immuthera" OR "imunen" OR "imuprin" OR "imurane" OR "imurek" OR "imuren" OR "nsc 39084" OR "nsc39084" OR "thioazeprine" OR "thioprine" OR "transimune" OR "zytrim" OR "imidazole" OR "nitroimidazole")</p>
Indexes=BIOSIS Previews Timespan=All years		

CDSR

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to March 2014>

Search Strategy:

-
- 1 (azathioprine or thiopurine* or imurel or immuran or imuran or "6 (1 methyl 4 nitro 5 imidazolyl) mercaptopurine" or arathioprin* or aza-q or azafalk or azahexal or azamedac or azamun* or azanin or azapin or azapress or azaprine or azarex or azasan or azathiodura or azathipine or azathiopurine or azathropsin or azatioprina or azatrox or azatrimel or azopi or azoran or azothioprin or "bw 57 322" or bw57322 or "bw57-322" or "bw 57322" or colinsan or immuthera or imunen or imuprin or imurane or imurek or imuren or "nsc 39084" or nsc39084 or thioazepine or thioprine or transimune or zytrim or imidazole or nitroimidazole).mp. (224)
 - 2 (thiopurine* or thioguanin* or tioguan* or "2 amino 6 purinethiol" or tabloid or "6 thioguanin*" or lanvis or "2 amino 6 mercaptopurine" or "2 amino purine 6 thiol" or "2 aminopurine 6 thiol" or "6 mercaptoguanine" or "6 thioquanine" or "nsc 752" or nsc752 or thioguanidine).mp. (17)
 - 3 ("6-mercaptopurine" or "6 mercaptopurine" or "6 mercapto purine" or "6 mercaptopurin" or "6 mercaptopurin monohydrate" or mercaptopurin* or thiopurine* or "6-thiopurine" or leupurin* or "bw 57323h" or "6 thiohypoxanthine" or "6-thiohypoxanthine" or "monohydrate puri-nethol" or "bw 57 323h" or "puri nethol" or purimethol or purinethol or "bw 57-323h" or "17-dihydro-6h-purine-6-thione mercaptopurine" or "6 mp" or "6 purinethiol" or "6 purinethiol hydrate" or classen or empurine or ismipur or leukerin or loulla or mercaleukin or mercapurene or mern or mycaptine or "nsc 755" or nsc755 or "purine 6 thiol" or "purine thiol (6)" or purinethiol or thiohypoxanthine or xaluprine).mp. (86)
 - 4 or/1-3 (256)
 - 5 (methyltransferases or "thiopurine methyltransferase*" or "thiopurine s methyltransferase*" or "e.c. 2.1.1.67" or tpmt).mp. (4)
 - 6 4 and 5 [***tpmt AND any drug***] (4)
 - 7 (phenotype or "high pressure liquid chromatography" or hplc or "clinical laboratory techniques" or "clinical chemistry tests" or "cytological techniques" or "hematologic tests" or "radioligand assay" or "analytical chemistry techniques" or "enzyme assays" or "clinical enzyme tests" or "mass spectrometry" or "tandem mass spectrometry" or "chromatography" or "liquid chromatography" or "high adj3 liquid adj3 chromatograph*" or "cytologic* techniq*" or "cytologic* technic*" or (hematolog* adj2 (test or tests or testing)) or (haematolog* adj2 (test or tests or testing)) or "blood adj1 (test or tests or testing)" or radioassay* or radioreceptor* or radioligand*).mp. (136)
 - 8 (pharmacogenetics or genetics or "genetic testing" or "heterozygote detection" or genotype or "sequence analysis" or heterozygote or homozygote or hemizygote or "genetic techniques" or "genetic association studies" or "genome-wide association study" or "genetic testing" or "genotyping techniques" or "restriction mapping" or "restriction fragment length polymorphism" or "single-stranded conformational polymorphism" or "oligonucleotide array sequence analysis" or "polymerase chain reaction" or "pharmacological biomarkers" or "genetic markers" or "biological markers" or "genetic predisposition to disease" or "amplification refractory mutation system" or microchip or pharmacogen* or toxicogen* or ((genotyp* or genetic*) adj2 (test or tested or tests or testing or predispos* or screen*)) or biomarker* or PCR).mp. (728)
 - 9 7 or 8 [***pheno OR geno***] (813)
 - 10 6 and 9 [***S9: (tpmt AND any drug) AND ((pheno OR geno)***)] (2)

CCRT

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <January 2014>

Search Strategy:

-
- 1 Azathioprine/ or (thiopurine* or azathioprine or azothioprine or imurel or immuran or imuran or "6 (1 methyl 4 nitro 5 imidazolyl)mercaptapurine" or arathioprin* or aza-q or azafalk or azahexal or azamedac or azamun* or azanin or azapin or azapress or azaprime or azarex or azasan or azathiodura or azathipine or azathiopurine or azathropsin or azatioprina or azatrox or azatrimem or azopi or azoran or azothioprin or "bw 57 322" or bw57322 or "bw57-322" or "bw 57322" or colinsan or immuthera or imunen or imuprin or imurane or imurek or imuren or "nsc 39084" or nsc39084 or thioazeprine or thioprine or transimune or zytrim or imidazole or nitroimidazole).mp. (2152)
 - 2 Thioguanine/ or (thiopurine* or thioguanin* or tioguan* or "2 amino 6 purinethiol" or tabloid or "6 thioguanine" or tioguanine or "6 thioguanine" or lanvis or "2 amino 6 mercaptopurine" or "2 amino purine 6 thiol" or "2 aminopurine 6 thiol" or "6 mercaptoguanine" or "6 thioquanine" or "nsc 752" or nsc752 or thioguanidine).mp. (329)
 - 3 6-Mercaptopurine/ or ("6-thiopurine" or leupurin or "bw 57323h" or "bw 57 323h" or "bw 57-323h" or "6 mercaptopurine" or "6-mercaptopurine" or "6 thiohypoxanthine" or "6-thiohypoxanthine" or "puri-nethol" or "puri nethol" or "purimethol" or "purinethol" or mercaptopurin* or "17-dihydro-6h-purine-6-thione mercaptopurine" or thiopurine* or "monohydrate puri-nethol" or "6 mercapto purine" or "6 mercaptopurin" or "6 mercaptopurin monohydrate" or "6 mp" or "6 purinethiol" or "6 purinethiol hydrate" or classen or empurine or ismipur or leukerin or leupurine or loulla or mercapleukin or mercapurene or mern or mycaptine or "nsc 755" or nsc755 or "purine 6 thiol" or "purine thiol (6)" or purinethiol or thiohypoxanthine or xaluprine).mp. (445)
 - 4 or/1-3 (2739)
 - 5 exp Methyltransferases/ or ("thiopurine methyltransferase*" or "thiopurine s methyltransferase" or "e.c. 2.1.1.67" or tpmt).mp. (236)
 - 6 4 and 5 [***any drug AND tpmt***] (30)
 - 7 Chemistry Techniques, Analytical/ or Chromatography/ or Chromatography, High Pressure Liquid.mp. or Chromatography, Liquid/ or Clinical Chemistry/ or Clinical Chemistry Tests/ or Clinical Enzyme Tests/ or Clinical Laboratory Techniques/ or exp Cytological techniques/ or Enzyme Assays/ or exp Hematologic Tests/ or Mass Spectrometry/ or Phenotype/ or Radioligand Assay/ or Tandem Mass Spectrometry/ or ("cytologic* techniq*" or "cytologic* technic*" or (clinic* lab* adj2 (technic* or techniq*)) or "clinic* chemistry" or "high adj3 liquid adj3 chromatograph*" or hplc or (hematolog* adj2 (test or tests or testing)) or (haematolog* adj2 (test or tests or testing)) or (blood adj1 (test or tests or testing)) or "liquid adj1 chromatograph*" or phenotype* or radioassay* or radioreceptor* or radioligand* or ((spectrometry or spectroscopy or spectrum) adj1 mass)).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword] (25845)
 - 8 Biological Markers/ or Biomarkers, Pharmacological/ or Genomics/ or Gene expression/ or Genetic Association Studies/ or Genome-Wide Association Study/ or Genetic Markers/ or Genetic Variation/ or Genetics, Medical/ or Genetic Predisposition to Disease/ or Genetics/ or Genetics, Population/ or Genetic Testing/ or Genetic Techniques/ or Genotype/ or Genotyping Techniques/ or Genetic/ or Polymorphism/ or Haplotypes/ or Heterozygote/ or Heterozygote Detection/ or Hemizygote/ or Homozygote/ or Ligase Chain Reaction/ or Microchip Analytical Procedures/ or Mutation/ or Nucleic Acid Amplification Techniques/ or Nucleic Acid Denaturation/ or Nucleotide Mapping/ or exp Peptide Mapping/ or Pharmacogenetics/ or exp Polymerase Chain Reaction/ or Polymorphism, Restriction Fragment Length/ or Polymorphisms, Single Nucleotide/ or Polymorphisms, Single-Stranded Conformational/ or Population Characteristics/ or exp Restriction Mapping/ or exp Sequence Analysis/ or Toxicogenetics/ or (Genome* or "genetic marker" or (genetic adj1 (variation or variety)) or (genetic* adj1 (susceptibility or predisposition)) or "population genetics" or ((genetic* or genom*) adj1 (technic* or techniq*)) or "genetic carrier*" or Heterozygote* or Hemizygote* or Homozygote* or microchip or Pharmacogen* or rflp or rflps or snps or sscp or heterogeneity or (restriction adj2 (mapping or analysis)) or toxicogen* or "Amplification Refractory Mutation System" or ((genotyp* or genetic*) adj2 (test or tested or tests or testing) or predispos* or screen*)) or biomarker* or PCR).mp. (18489)

9 7 or 8 [***pheno OR geno***] (42039)

10 6 and 9 [***(tpmt AND any drug) AND (pheno OR geno)***] (16)

CINAHL

S6 AND S9 – 37

S9 - S7 OR S8 - 164,241

S8 - ((MH "Genotype") OR (MH "Oligonucleotide Array Sequence Analysis") OR (MH "Microchip Analytical Procedures") OR (MH "Microarray Analysis") OR (MH "Nucleotide Mapping") OR (MH "Peptide Mapping") OR (MH "Maximum Tolerated Dose") OR (MH "Toxicity Tests") OR (MH "Pharmacogenetics") OR (MH "Genetics") OR (MH "Genetics, Medical") OR (MH "Genes") OR (MH "Gene Expression") OR (MH "Genome") OR (MH "Genome, Human") OR (MH "Alleles") OR (MH "Mutation") OR (MH "Gene Amplification") OR (MH "Genetic Markers") OR (MH "Polymorphism, Genetic") OR (MH "Genetic Screening") OR (MH "Genetic Techniques") OR (MH "Chromosome Mapping") OR (MH "Cytogenetic Analysis") OR (MH "Gene Expression Profiling") OR (MH "Molecular Diagnostic Techniques") OR (MH "Nucleic Acid Amplification Techniques") OR (MH "Polymerase Chain Reaction+") OR (MH "Sequence Analysis" OR (MH "Random Amplified Polymorphic DNA Technique" OR (MH "Biological Markers")))) OR (TX ("heterozygote" OR "homozygote" OR "hemizygote" OR "genetic association studies" OR "restriction mapping" OR "single stranded conformational polymorphism" OR "biomarkers" OR "genetic predisposition" OR "microchip" OR "toxicogen*" OR "pharmacogen*" OR "genotype test" OR "genotype tests" OR "genotype testing" OR "genotype screen*" OR "PCR" OR "biomarker*" OR "amplification refractory mutation system")) - 79,036S7 - ((MH "Phenotype") OR (MH "Chromatography, High Pressure Liquid") OR (MH "Chromatography, Liquid") OR (MH "Chemistry, Clinical") OR (MH "Enzyme Tests") OR (MH "Diagnosis, Laboratory") OR (MH "Cytodiagnosis") OR (MH "Hematologic Tests+") OR (MH "Chemistry, Analytical") OR (MH "Mass Spectrometry+") OR (MH "Cytological Techniques+") OR (MH "Cytological Techniques, Automated") OR (MH "Enzymes, Coenzymes, Enzyme Inhibitors (Non-Cinahl+)") OR (MH "Chromatography")) OR (TX ("phenotype" OR "high pressure liquid chromatography" OR "hplc" OR "radioligand assay" OR "tandem mass spectrometry" OR "high adj3 liquid adj3 chromatograph*" OR "cytologic* techniq*" OR "cytologic* technic*" OR "(hematolog* adj2 (test OR tests OR testing))" OR "(haematolog* adj2 (test OR tests OR testing))" OR "blood adj1 (test OR tests OR testing)" OR "radioassay*" OR "radioreceptor*" OR "radioligand*")) - 108,362

S6 - (S1 OR S2 OR S3) AND (S4) – 45

S5 - S1 OR S2 OR S3 - 1,125

S4 - (TX ("thiopurine methyltransferase" OR "methyltransferase" OR "methyltransferase*" OR "thiopurine methyltransferase*" OR "thiopurine s methyltransferase*" OR "e.c. 2.1.1.67" OR tpmt)) – 339

S3 - (MH "6-Mercaptopurine") OR (TX ("6-mercaptopurine" OR "6 mercaptopurine" OR "6 mercapto purine" OR "6 mercaptopurin" OR "6 mercaptopurin monohydrate" OR mercaptopurin* OR thiopurine* OR "6-thiopurine" OR leupurin* OR "bw 57323h" OR "6 thiohypoxanthine" OR "6-thiohypoxanthine" OR "monohydrate puri-nethol" OR "bw 57 323h" OR "puri nethol" OR purimethol OR purinethol OR "bw 57-323h" OR "17-dihydro-6h-purine-6-thione mercaptopurine" OR "6 mp" OR "6 purinethiol" OR "6 purinethiol hydrate" OR classen OR empurine OR ismipur OR leukerin OR loulla OR mercalleukin OR mercapurene OR mern OR mycaptine OR "nsc 755" OR nsc755 OR "purine 6 thiol" OR "purine thiol (6)" OR purinethiol OR thiohypoxanthine OR xaluprine)) – 387

S2 - (TX ("thioguanine" OR "tioguanine" OR "thiopurine*" OR thioguanin* OR tioguan* OR "2 amino 6 purinethiol" OR tabloid OR "6 thioguanin*" OR lanvis OR "2 amino 6 mercaptopurine" OR "2 amino purine 6 thiol" OR "2 aminopurine 6 thiol" OR "6 mercaptoguanine" OR "6 thioquanine" OR "nsc 752" OR nsc752 OR thioguanidine)) – 43

S1 - (MH "Azathioprine") OR (TX ("azathioprine" or "thiopurine" or imurel or immuran or imuran or "6 (1 methyl 4 nitro 5 imidazolyl mercaptopurine" or arathioprin* or "aza-q" or azafalk OR azahexal OR azamedac OR azamun* OR azanin OR azapin OR azapress OR azaprine OR azarex OR azasan OR azathiodura OR azathipine OR azathiopurine OR azathropsin OR azatioprina OR azatrox OR azatrimem OR azopi OR azoran OR azothioprin OR "bw 57 322" OR bw57322 OR "bw57-322" OR "bw 57322" OR "colinsan OR immuthera OR imunen OR imuprin OR imurane OR imurek OR imuren" OR "nsc 39084" OR nsc39084 OR thioazeprine OR thioprine OR transimune OR zytrim OR imidazole OR nitroimidazole)) - 846

DARE

- 1 thiopurine.mp. [mp=title, full text, keywords] (7)
- 2 tpmt.mp. [mp=title, full text, keywords] (0)
- 3 thiopurine s-methyltransferase.mp. [mp=title, full text, keywords] (1)
- 4 (Methyltransferases or ("thiopurine methyltransferase*" or "thiopurine s methyltransferase" or "e.c. 2.1.1.67" or tpmt)).mp. [mp=title, full text, keywords] (3)
- 5 (Methyltransferases or ("thiopurine methyltransferase*" or "thiopurine s methyltransferase" or "e.c. 2.1.1.67" or tpmt or thiopurine)).mp. [mp=title, full text, keywords] (7)

EMBASE

Database: Embase <1980 to 2014 Week 14>

Search Strategy:

-
- 1 Thiopurine methyltransferase/ or ("e.c. 2.1.1.67" or "thiopurine s methyltransferase" or "thiopurine s-methyltransferase" or "tpmt").mp. (2105)
 - 2 Azathioprine/ or Azathioprine derivative/ or ("6 (1 methyl 4 nitro 5 imidazolyl)mercaptapurine" or arathioprin* or aza-q or azafalk or azahexal or azamedac or azamun or azamune or azanin or azapin or azapress or azaprine or azarex or azasan or azathiodura or azathioprine or azathioprim or azathioprine or "azathioprine sodium" or azathiopurine or azathropsin or azatioprina or azatox or azatrimem or azopi or azoran or azothioprin or azathioprine or "bw 57 322" or "bw 57-322" or "bw 57322" or "bw57-322" or bw57322 or colinsan or immuran or immurel or immuthera or imunen or imuprin or Imuran or imurane or imurek or imurel or imuren or "nsc 39084" or nsc39084 or thioazeprine or thioprine or transimune or zytrim).mp. (71150)
 - 3 Tioguanine/ or Guanine derivative/ or ("2 amino 6 mercaptopurine" or "2 amino 6 purinethiol" or "2 amino purine 6 thiol" or "2 aminopurine 6 thiol" or "6 mercaptopurine" or "6 thioguanine" or "6 thioquanine" or lanvis or "nsc 752" or nsc752 or thioguanidine or thioguanine).mp. (9913)
 - 4 Mercaptopurine/ or 6-mercaptapurine derivative/ or ("6 mercapto purine" or "6 mercaptopurin" or "6 mercaptopurine" or "6 mercaptopurine monohydrate" or "6 mp" or "6 purinethiol" or "6 purinethiol hydrate" or "6 thiohypoxanthine" or "6 thiopurine" or "6-mercaptapurine" or classen or empurine or ismipur or leukerin or leupurin* or loulla or mercaleukin or mercaptopurin* or mercapurene or mern or mycaptine or "nsc 755" or nsc755 or "puri nethol" or "puri-nethol" or "purine 6 thiol" or "purine thiol (6)" or purinethiol or purinethol or thiohypoxanthine or thiopurine or xaluprine).mp. (21152)
 - 5 2 or 3 or 4 [***any drug***] (91269)
 - 6 1 and 5 [***tpmt AND any drug] (2046)
 - 7 Analysis/ or Assay/ or Blood chemistry/ or Blood examination/ or Chemical analysis/ or Chromatography/ or Clinical chemistry/ or Cytology/ or Diagnosis/ or Diagnostic approach route/ or Diagnostic procedure/ or Enzymatic assay/ or Enzyme analysis/ or Enzyme assay/ or Genotype phenotype correlation/ or Hemoglobin analysis/ or High performance liquid chromatography/ or Liquid chromatography/ or Measurement/ or Phenotype/ or Phenotype variation/ or Radioassay/ or Radiochemsity/ or Radioenzymatic assay/ or Screening/ or Mass spectrometry/ or Tandem mass spectrometry/ or ("phenotyp* adj1 (varia* or correlat*)" or "high adj3 liquid adj3 chromatograph*" or hplc or chromatograph* or ((diagnos* or lab* or "clinic* chem*" or cytologic*) adj1 (method* or procedure* or technic* or techniq* or analys* or screen* or tool or investigat* or sign or physical or test or tests or testing)) or "enzyme* adj2 (assay* or test or tests or testing or determin* or character* or analys*)" or ((hematolo* or haematolog* or blood) adj2 (test or tests or testing)) or (spectr* adj3 mass) or radioassay* or radioligand* or "(radiochemical or radioenzym*)" adj1 (assay* or analys*)" or "chem* adj1 (clinic* or study or analyt* or pharmaceut*)" or "clinicochemical analysis").mp. (2904340)
 - 8 Amplified fragment length polymorphism/ or Biological marker/ or Chromosome analysis/ or Clinical genetics/ or DNA determination/ or DNA extraction/ or DNA isolation/ or DNA marker/ or DNA polymorphism/ or DNA restriction/ or DNA screening/ or Gene amplification/ or Gene expression profiling/ or Gene identification/ or Gene isolation/ or Gene mapping/ or Gene identification/ or Genetic analysis/ or Genetic association/ or Genetic correlation/ or Genetic heterogeneity/ or Genetic line/ or Genetic marker/ or Genetic organization/ or Genetic polymorphism/ or Genetic predisposition/ or Genetic procedures/ or Genetic screening/ or Genetic susceptibility/ or Genetic trait/ or Genotype/ or Genetics/ or Genome/ or Genome analysis/ or Genotyping technique/ or Hemizygoty/ or Hemizygote/ or Heterozygoty/ or Heterozygote/ or Heterozygote detection/ or High pressure liquid chromatography/ or Homozygoty/ or Homozygote/ or Human genetics/ or Liquid chromatography/ or Marker chromosome/ or Marker gene/ or Mass spectrometry/ or Microchip analysis/ or Mutation/ or Mutational analysis/ or Sequence analysis/ or High throughput sequencing/ or Restriction mapping/ or Restriction fragment length polymorphism/ or Restriction fragment length polymorphism/ or Single nucleotide polymorphism/ or Nucleic acid analysis/ or Inverse polymerase chain reaction/ or Ligase chain reaction/ or Medical genetics/ or Multiplex polymerase chain reaction/ or Nucleic acid amplification/ or Nucleic acid analysis/ or Nucleic acid sequence based

amplification/ or Nucleotide sequence/ or Polymerase chain reaction/ or Serial analysis of gene expression/ or Single strand conformation polymorphism/ or Spectrometry/ or Real time polymerase chain reaction/ or Restriction fragment length polymorphism/ or Reverse transcription polymerase chain reaction/ or RNA analysis/ or Pharmacogenetics/ or Pharmacological biomarker/ or Polymerase chain reaction/ or Population genetics/ or Toxicogenetics/ or (pharmacogen* or ((genetic* or genom* or gene or genotyp*) adj2 (test or tests or testing or effect or determin* or factor or phenomena or process* or line or correlat* or heterogen* or organiz* or character* or trait* or component* or alterat* or mutat* or screen* or detect* or techniq* or technic* or map* or assay* or polymorph* or marker* or predispos* or prognos* or susceptib* or associat*)) or eugenic* or (analys* adj2 (chromosom* or cytogen* or sequenc*)) or RFLP or PCR or biomarker* or bioindicator* or microchip).mp. (2825723)

9 7 or 8 [***pheno OR geno***] (4922431)

10 6 and 9 [***S9: (tpmt AND any drug) AND ((pheno OR geno)***] (1640)

HTA

Database: EBM Reviews - Health Technology Assessment <1st Quarter 2014>

Search Strategy:

-
- 1 Azathioprine/ or (azathioprine* or thiopurine* or imurel or immuran or imuran or "6 (1 methyl 4 nitro 5 imidazolyl) mercaptopurine" or arathioprin* or aza-q or azafalk or azahexal or azamedac or azamun* or azanin or azapin or azapress or azaprime or azarex or azasan or azathiodura or azathipine or azathiopurine or azathropsin or azatioprina or azatrox or azatrimem or azopi or azoran or azothioprin or "bw 57 322" or bw57322 or "bw57-322" or "bw 57322" or colinsan or immuthera or imunen or imuprin or imurane or imurek or imuren or "nsc 39084" or nsc39084 or thioazeprine or thioprine or transimune or zytrim or imidazole or nitroimidazole).mp. (10)
 - 2 Thioguanine/ or (thiopurine* or thioguanin* or tioguan* or "2 amino 6 purinethiol" or tabloid or "6 thioguanin*" or lanvis or "2 amino 6 mercaptopurine" or "2 amino purine 6 thiol" or "2 aminopurine 6 thiol" or "6 mercaptoguanine" or "6 thioquanine" or "nsc 752" or nsc752 or thioguanidine).mp. (4)
 - 3 6-Mercaptopurine/ or ("1,7-dihydro-6h-purine-6-thione" or "6-mercaptopurine" or "6 mercaptopurine" or "6 mercapto purine" or "6 mercaptopurin" or "6 mercaptopurin monohydrate" or mercaptopurin* or thiopurine* or "6-thiopurine" or leupurin* or "bw 57323h" or "6 thiohypoxanthine" or "6-thiohypoxanthine" or "monohydrate puri-nethol" or "bw 57 323h" or "puri nethol" or purimethol or purinethol or "bw 57-323h" or "17-dihydro-6h-purine-6-thione mercaptopurine" or "6 mp" or "6 purinethiol" or "6 purinethiol hydrate" or classen or empurine or ismipur or leukerin or loulla or mercaleukin or mercapurene or mern or mycaptine or "nsc 755" or nsc755 or "purine 6 thiol" or "purine thiol (6)" or purinethiol or thiohypoxanthine or xaluprine).mp. (6)
 - 4 or/1-3 (11)
 - 5 Methyltransferases/ or (methyltransferase* or transferase* or "thiopurine methyltransferase*" or "thiopurine s methyltransferase*" or "e.c. 2.1.1.67" or tpmt).mp. (9)
 - 6 ((Analytical Chemistry/ or Chromatography/ or Chromatography, High Pressure Liquid/ or Chromatography, Liquid/ or Clinical Chemistry/ or Clinical Laboratory Techniques/ or Clinical Chemistry Tests/ or Cytological Techniques/ or Hematologic Tests/ or Laboratory Techniques.mp.) and Procedures/ or Mass spectrometry/ or Molecular Diagnostic Techniques/ or Phenotype/ or Radioligand Assay/ or Tandem Mass Spectrometry/ or (somatotypes or "liquid chromatography" or "high adj3 liquid adj3 chromatograph*" or hplc or "clinic* lab*techni*" or "cytologic* techniq*" or "cytologic* technic*" or "molecular diagnostic*" or ("analytic* chemistry" or "clinical enzyme tests" or "clinic* chemistry tests" or "chromatography" or "liquid chromatography" or "high adj3 liquid adj3 chromatograph*" or "enzyme assays" or (hematolog* adj2 (test or tests or testing)) or (haematolog* adj2 (test or tests or testing)) or "blood adj1 (test or tests or testing)" or (lab* adj1 (diagnos* or exam* or procedure* or techniq* or technic*)) or "mass spectrometry" or "protein-binding radioassay" or radioreceptor* or ((spectrometry or spectroscopy or spectrum) adj1 mass) or radioassay* or "radioligand*or tandem mass spectrometry").mp. [mp=title, text, subject heading word] (78)
 - 7 Biological Markers/ or Chromosome Mapping/ or Cytogenetics/ or Cytogenetic Analysis/ or Genome/ or Gene Expression Profiling/ or Genetic Heterogeneity/ or Genome, Human/ or Genetic Markers/ or Genetic Predisposition to Disease/ or Genetic Markers/ or Genetics, Medical/ or Gene expression/ or Genomics/ or Genetic Screening/ or Genetics/ or Genetics, Population/ or Genetic Techniques/ or Genotype/ or Haplotypes/ or Heterozygote/ or Heterozygote detection/ or Homozygote/ or Ligase Chain Reaction/ or Microchip Analytical Procedures/ or Molecular Diagnostic Techniques/ or Mutation/ or Nucleic Acid Amplification Techniques/ or Nucleic Acid Denaturation/ or Nucleotide Mapping/ or Peptide Mapping/ or Polymerase Chain Reaction/ or Polymorphism, Genetic/ or Polymorphism, Restriction Fragment Length/ or Polymorphisms, Single Nucleotide/ or Polymorphisms, Single-Stranded Conformational/ or Pharmacogenetics/ or Restriction Mapping/ or Sequence Analysis/ or "Variation, Genetics"/ or ("amplification refractory mutation system" or biomarker* or gene* or genom* or ((genotyp* or genetic*) adj2 (carrier or test or tested or tests or testing or technic* or techniq* or mapping or polymorphism or predispos* or screen* or susceptib*)) or hemizygote or microchip or pharmacogen* or "restriction fragment length " or toxicogen* or PCR or "Restriction adj1 (mapping or analysis)" or "Sequence adj1 (determin* or analy*)").mp. (1564)

- 8 6 or 7 (1610)
- 9 5 and 4 [***tpmt AND any drug***] (4)
- 10 8 and 9 [***(tpmt AND any drug) AND (pheno OR geno)***] (4)

IPA

Database: International Pharmaceutical Abstracts <1970 to March 2014>

Search Strategy:

-
- 1 (azathioprine or thiopurine* or imurel or immuran or imuran or "6 (1 methyl 4 nitro 5 imidazolyl) mercaptopurine" or arathioprin* or aza-q or azafalk or azahexal or azamedac or azamun* or azanin or azapin or azapress or azaprime or azarex or azasan or azathiodura or azathipine or azathiopurine or azathropsin or azatioprina or azatrox or azatrimem or azopi or azoran or azothioprin or "bw 57 322" or bw57322 or "bw57-322" or "bw 57322" or colinsan or immuthera or imunen or imuprin or imurane or imurek or imuren or "nsc 39084" or nsc39084 or thioazeprine or thioprine or transimune or zytrim or imidazole or nitroimidazole).mp. (1986)
 - 2 (thiopurine* or thioguanin* or tioguan* or "2 amino 6 purinethiol" or tabloid or "6 thioguanin*" or lanvis or "2 amino 6 mercaptopurine" or "2 amino purine 6 thiol" or "2 aminopurine 6 thiol" or "6 mercaptoguanine" or "6 thioquanine" or "nsc 752" or nsc752 or thioguanidine).mp. (267)
 - 3 ("6-mercaptopurine" or "6 mercaptopurine" or "6 mercapto purine" or "6 mercaptopurin" or "6 mercaptopurin monohydrate" or mercaptopurin* or thiopurine* or "6-thiopurine" or leupurin* or "bw 57323h" or "6 thiohypoxanthine" or "6-thiohypoxanthine" or "monohydrate puri-nethol" or "bw 57 323h" or "puri nethol" or purimethol or purinethol or "bw 57-323h" or "17-dihydro-6h-purine-6-thione mercaptopurine" or "6 mp" or "6 purinethiol" or "6 purinethiol hydrate" or classen or empurine or ismipur or leukerin or loulla or mercaleukin or mercapurene or mern or mycaptine or "nsc 755" or nsc755 or "purine 6 thiol" or "purine thiol (6)" or purinethiol or thiohypoxanthine or xaluprine).mp. (538)
 - 4 (methyltransferases or "thiopurine methyltransferase*" or "thiopurine s methyltransferase*" or "e.c. 2.1.1.67" or tpmt).mp. (108)
 - 5 1 or 2 or 3 [***any drug***] (2389)
 - 6 4 and 5 [***tpmt AND any drug***] (91)
 - 7 (phenotype or "high pressure liquid chromatography" or hplc or "clinical laboratory techniques" or "clinical chemistry tests" or "cytological techniques" or "hematologic tests" or "radioligand assay" or "analytical chemistry techniques" or "enzyme assays" or "clinical enzyme tests" or "mass spectrometry" or "tandem mass spectrometry" or "chromatography" or "liquid chromatography" or "high adj3 liquid adj3 chromatograph*" or "cytologic* techniq*" or "cytologic* technic*" or (hematolog* adj2 (test or tests or testing)) or (haematolog* adj2 (test or tests or testing)) or "blood adj1 (test or tests or testing)" or radioassay* or radioreceptor* or radioligand*).mp. (33942)
 - 8 (pharmacogenetics or genetics or "genetic testing" or "heterozygote detection" or genotype or "sequence analysis" or heterozygote or homozygote or hemizygote or "genetic techniques" or "genetic association studies" or "genome-wide association study" or "genetic testing" or "genotyping techniques" or "restriction mapping" or "restriction fragment length polymorphism" or "single-stranded conformational polymorphism" or "oligonucleotide array sequence analysis" or "polymerase chain reaction" or "pharmacological biomarkers" or "genetic markers" or "biological markers" or "genetic predisposition to disease" or "amplification refractory mutation system" or microchip or pharmacogen* or toxicogen* or ((genotyp* or genetic*) adj2 (test or tested or tests or testing or predispos* or screen*)) or biomarker* or PCR).mp. (8729)
 - 9 7 or 8 [***pheno OR geno***] (41900)
 - 10 6 and 9 [***S9: (tpmt AND any drug) AND ((pheno OR geno)***)] (68)

Medline

Database: Ovid MEDLINE(R) <1946 to March Week 4 2014>

Search Strategy:

-
- 1 Methyltransferases/ or ("thiopurine methyltransferase*" or "thiopurine s methyltransferase" or "e.c. 2.1.1.67" or tpmt).mp. (9436)
 - 2 Azathioprine/ or (thiopurine* or azathioprine or imurel or immuran or imuran or "6 (1 methyl 4 nitro 5 imidazolyl)mercaptapurine" or arathioprin* or aza-q or azafalk or azahexal or azamedac or azamun* or azanin or azapin or azapress or azaprime or azarex or azasan or azathiodura or azathipine or azathiopurine or azathropsin or azatioprina or azatrox or azatrimem or azopi or azoran or azothioprin or "bw 57 322" or bw57322 or "bw57-322" or "bw 57322" or colinsan or immuthera or imunen or imuprin or imurane or imurek or imuren or "nsc 39084" or nsc39084 or thioazeprine or thioprine or transimune or zytrim or imidazole or nitroimidazole).mp. (34847)
 - 3 Thioguanine/ or (thiopurine* or thioguanin* or tioguan* or "2 amino 6 purinethiol" or tabloid or "6 thioguanin*" or lanvis or "2 amino 6 mercaptopurine" or "2 amino purine 6 thiol" or "2 aminopurine 6 thiol" or "6 mercaptoguanine" or "6 thioquanine" or "nsc 752" or nsc752 or thioguanidine).mp. (5145)
 - 4 6-Mercaptopurine/ or (thiopurine* or "6-thiopurine" or leupurin* or "bw 57323h" or "6 mercaptopurine" or "6 thiohypoxanthine" or "6-mercaptopurine" or "monohydrate puri-nethol" or "6-thiohypoxanthine" or "bw 57 323h" or "puri nethol" or purimethol or purinethol or "bw 57-323h" or mercaptopurina or "17-dihydro-6h-purine-6-thione mercaptopurine" or "6 mercapto purine" or "6 mercaptopurin" or "6 mercaptopurin monohydrate" or "6 mp" or "6 purinethiol" or "6 purinethiol hydrate" or classen or empurine or ismipur or leukerin or loulla or mercaleukin or mercaptopurin or mercapurene or mern or mycaptine or "nsc 755" or nsc755 or "purine 6 thiol" or "purine thiol (6)" or purinethiol or thiohypoxanthine or xaluprine).mp. (7718)
 - 5 1 or 2 or 3 or 4 [***tpmt OR any drug***] (50899)
 - 6 2 or 3 or 4 [***any drug***] (42576)
 - 7 1 and 6 [***tpmt AND any drug***] (1113)
 - 8 exp Phenotype/ or Chromatography, High Pressure liquid/ or Clinical Laboratory Techniques/ or Clinical Chemistry Tests/ or Cytological Techniques/ or Hematologic Tests/ or Radioligand Assay/ or Chemistry Techniques, Analytical/ or Enzyme Assays/ or Clinical enzyme tests/ or Mass spectrometry/ or Tandem Mass Spectrometry/ or Chromatography/ or Chromatography, High Pressure Liquid/ or Chromatography, Liquid/ or ("high adj3 liquid adj3 chromatograph*" or hplc or "cytologic* techniq*" or "cytologic* technic*" or (hematolog* adj2 (test or tests or testing)) or (haematolog* adj2 (test or tests or testing)) or "blood adj1 (test or tests or testing)" or radioassay* or radioreceptor* or radioligand*).mp. (611828)
 - 9 Pharmacogenetics/ or Genetics/ or Genetic Testing/ or Heterozygote detection/ or Genotype/ or exp Sequence Analysis/ or Heterozygote/ or Homozygote/ or Hemizygote/ or genetic techniques/ or genetic association studies/ or genome-wide association study/ or genetic testing/ or genotyping techniques/ or Restriction Mapping/ or Polymorphism, Restriction Fragment Length/ or Polymorphism, Single-Stranded Conformational/ or Oligonucleotide Array Sequence Analysis/ or exp Polymerase Chain Reaction/ or Biomarkers, Pharmacological/ or Genetic Markers/ or Biological Markers/ or genetic predisposition to disease/ or ("Amplification Refractory Mutation System" or microchip or pharmacogen* or toxicogen* or ((genotyp* or genetic*) adj2 (test or tested or tests or testing or predispos* or screen*)) or biomarker* or PCR).mp. (1200911)
 - 10 8 or 9 [***pheno OR geno***] (1676988)
 - 11 8 and 9 [***pheno AND geno***] (135751)
 - 12 ((Evaluation Studies/ or Comparative Study/ or Validation Studies/ or exp Sensitivity/) and Specificity/) or Predictive Value of Tests/ or Diagnostic Errors/ or False Negative Reactions/ or False Positive Reactions/ or Observer Variation/ or (sensitivity or specificity or "positive predictive value" or "negative predictive value" or accuracy).mp. (1492650)
 - 13 11 or 12 [***(pheno AND geno) or accuracy***] (1609568)

14 10 or 12 [***(pheno OR geno) OR accuracy***] (2923259)
15 10 and 12 [***(pheno OR geno) AND accuracy***] (246379)
16 11 and 12 [***(pheno AND geno) AND accuracy***] (18833)
17 5 and 14 [***S1: (tpmt OR any drug) AND ((pheno OR geno) OR accuracy)***] (9276)
18 5 and 15 [***S2: (tpmt OR any drug) AND ((pheno OR geno) AND accuracy)***] (1049)
19 5 and 10 [***S3: (tpmt OR any drug) AND (pheno OR geno)***] (5496)
20 5 and 13 [***S4: (tpmt OR any drug) AND ((pheno AND geno) OR accuracy)***] (5202)
21 5 and 16 [***S5: (tpmt OR any drug) AND ((pheno AND geno) AND accuracy)***] (109)
22 5 and 11 [***S6: (tpmt OR any drug) AND ((pheno AND geno)***] (482)
23 7 and 14 [***S7: (tpmt AND any drug) AND ((pheno OR geno) OR accuracy)***] (736)
24 7 and 15 [***S8: (tpmt AND any drug) AND ((pheno OR geno) AND accuracy)***] (83)
25 7 and 10 [***S9: (tpmt AND any drug) AND ((pheno OR geno)***] (696)
26 7 and 13 [***S10: (tpmt AND any drug) AND ((pheno AND geno) OR accuracy)***] (252)
27 7 and 16 [***S11: (tpmt AND any drug) AND ((pheno AND geno) AND accuracy)***] (22)
28 7 and 11 [***S12: (tpmt AND any drug) AND ((pheno AND geno)***] (151)
29 1 and 14 [***S13: (tpmt) AND ((pheno OR geno) OR accuracy)***] (3854)
30 1 and 15 [***S14: (tpmt) AND ((pheno OR geno) AND accuracy)***] (598)
31 1 and 10 [***S15: (tpmt) AND ((pheno OR geno)***] (2559)
32 1 and 13 [***S16: (tpmt) AND ((pheno AND geno) OR accuracy)***] (2153)
33 1 and 16 [***S17: (tpmt) AND ((pheno AND geno) AND accuracy)***] (80)
34 1 and 11 [***S18: (tpmt) AND ((pheno AND geno)***] (340)
35 6 and 14 [***S19: (drug) AND ((pheno OR geno) OR accuracy)***] (6158)
36 6 and 15 [***S20: (drug) AND ((pheno OR geno) AND accuracy)***] (534)
37 6 and 10 [***S21: (drug) AND ((pheno OR geno)***] (3633)
38 6 and 13 [***S22: (drug) AND ((pheno AND geno) OR accuracy)***] (3301)
39 6 and 16 [***S23: (drug) AND ((pheno AND geno) AND accuracy)***] (51)
40 6 and 11 [***S24: (drug) AND ((pheno AND geno)***] (293)

NHSEED

Database: EBM Reviews - NHS Economic Evaluation Database <1st Quarter 2014>

Search Strategy:

-
- 1 Azathioprine/ or (azathioprine* or thiopurine* or imurel or immuran or imuran or "6 (1 methyl 4 nitro 5 imidazolyl) mercaptopurine" or arathioprin* or aza-q or azafalk or azahexal or azamedac or azamun* or azanin or azapin or azapress or azaprime or azarex or azasan or azathiodura or azathipine or azathiopurine or azathropsin or azatioprina or azatrox or azatrimem or azopi or azoran or azothioprin or "bw 57 322" or bw57322 or "bw57-322" or "bw 57322" or colinsan or immuthera or imunen or imuprin or imurane or imurek or imuren or "nsc 39084" or nsc39084 or thioazepine or thioprine or transimune or zytrim or imidazole or nitroimidazole).mp. (53)
 - 2 Thioguanine/ or (thiopurine* or thioguanin* or tioguan* or "2 amino 6 purinethiol" or tabloid or "6 thioguanin*" or lanvis or "2 amino 6 mercaptopurine" or "2 amino purine 6 thiol" or "2 aminopurine 6 thiol" or "6 mercaptoguanine" or "6 thioquanine" or "nsc 752" or nsc752 or thioguanidine).mp. (7)
 - 3 6-Mercaptopurine/ or ("1,7-dihydro-6h-purine-6-thione" or "6-mercaptopurine" or "6 mercaptopurine" or "6 mercapto purine" or "6 mercaptopurin" or "6 mercaptopurin monohydrate" or mercaptopurin* or thiopurine* or "6-thiopurine" or leupurin* or "bw 57323h" or "6 thiohypoxanthine" or "6-thiohypoxanthine" or "monohydrate puri-nethol" or "bw 57 323h" or "puri nethol" or purimethol or purinethol or "bw 57-323h" or "17-dihydro-6h-purine-6-thione mercaptopurine" or "6 mp" or "6 purinethiol" or "6 purinethiol hydrate" or classen or empurine or ismipur or leukerin or loulla or mercapleukin or mercapurene or mern or mycaptine or "nsc 755" or nsc755 or "purine 6 thiol" or "purine thiol (6)" or purinethiol or thiohypoxanthine or xaluprine).mp. (13)
 - 4 or/1-3 (56)
 - 5 Methyltransferases/ or (methyltransferase* or transferase* or "thiopurine methyltransferase*" or "thiopurine s methyltransferase*" or "e.c. 2.1.1.67" or tpmt).mp. (16)
 - 6 ((Analytical Chemistry/ or Chromatography/ or Chromatography, High Pressure Liquid/ or Chromatography, Liquid/ or Clinical Chemistry/ or Clinical Laboratory Techniques/ or Clinical Chemistry Tests/ or Cytological Techniques/ or Hematologic Tests/ or Laboratory Techniques.mp.) and Procedures/ or Mass spectrometry/ or Molecular Diagnostic Techniques/ or Phenotype/ or Radioligand Assay/ or Tandem Mass Spectrometry/ or (somatotypes or "liquid chromatography" or "high adj3 liquid adj3 chromatograph*" or hplc or "clinic* lab*techni*" or "cytologic* techniq*" or "cytologic* technic*" or "molecular diagnostic*" or ("analytic* chemistry" or "clinical enzyme tests" or "clinic* chemistry tests" or "chromatography" or "liquid chromatography" or "high adj3 liquid adj3 chromatograph*" or "enzyme assays" or (hematolog* adj2 (test or tests or testing)) or (haematolog* adj2 (test or tests or testing)) or "blood adj1 (test or tests or testing)" or (lab* adj1 (diagnos* or exam* or procedure* or techniq* or technic*)) or "mass spectrometry" or "protein-binding radioassay" or radioreceptor* or ((spectrometry or spectroscopy or spectrum) adj1 mass) or radioassay* or "radioligand*or tandem mass spectrometry")).mp. [mp=title, text, subject heading word] (255)
 - 7 Genetics/ or Biological Markers/ or Chromosome Mapping/ or Cytogenetics/ or Cytogenetic Analysis/ or Genome/ or Gene Expression Profiling/ or Genetic Heterogeneity/ or Genome, Human/ or Genetic Markers/ or Genetic Predisposition to Disease/ or Genetic Screening/ or Genetics, Population/ or Genetic Techniques/ or Genotype/ or Haplotypes/ or Heterozygote/ or Heterozygote detection/ or Homozygote/ or Ligase Chain Reaction/ or Microchip Analytical Procedures/ or Molecular Diagnostic Techniques/ or Mutation/ or Nucleic Acid Amplification Techniques/ or Nucleic Acid Denaturation/ or Nucleotide Mapping/ or Peptide Mapping/ or Polymerase Chain Reaction/ or Polymorphism, Genetic/ or Polymorphism, Restriction Fragment Length/ or Polymorphisms, Single Nucleotide/ or Polymorphisms, Single-Stranded Conformational/ or Pharmacogenetics/ or Restriction Mapping/ or Sequence Analysis/ or Variation, Genetics/ or ("amplification refractory mutation system " or biomarker* or gene* or genom* or ((genotyp* or genetic*) adj2 (carrier or test or tested or tests or testing or technic* or techniq* or mapping or polymorphism or predispos* or screen* or susceptib*)) or hemizygote or microchip or pharmacogen* or "restriction fragment length " or toxicogen* or PCR or "Restriction adj1 (mapping or analysis)" or "Sequence adj1 (determin* or analy*)").mp. (8381)
 - 8 6 or 7 (8434)

9 5 and 4 [***tpmt AND any drug***] (6)

10 8 and 9 [***(tpmt AND any drug) AND (pheno OR geno)***] (6)

PubMED

Recent queries in pubmed		
Search	Query	Items found
#259	Search (((("Methyltransferases"[Mesh] OR ("thiopurine methyltransferase"[Supplementary Concept] OR "Thiopurine S methyltransferase deficiency"[Supplementary Concept])) OR ("thiopurine methyltransferase"[All Fields] OR "thiopurine s methyltransferase"[All Fields] OR "thiopurine s-methyltransferase"[All Fields] OR (e.c.[All Fields] AND 2.1.1.67[All Fields]) OR "ec 2.1.1.67"[All Fields] OR "tpmt"[All Fields]))) AND (((("azothioprine"[All Fields] OR "imurel"[All Fields] OR "imuran"[All Fields] OR "immuran"[All Fields] OR "azathioprine"[All Fields] OR "thiopurine*"[All Fields] OR "6 (1 methyl 4 nitro 5 imidazolyl) mercaptopurine"[All Fields] OR (aza[All Fields] AND q[All Fields]) OR "azamun*"[All Fields] OR "azaprine"[All Fields] OR "ahasan"[All Fields] OR (azathio[All Fields] AND dura[All Fields]) OR "azathioprine"[All Fields] OR "azathiopurine"[All Fields] OR "azatrux"[All Fields] OR "azatrinem"[All Fields] OR "azodi"[All Fields] OR "azorean"[All Fields] OR (bw[All Fields] AND 57[All Fields] AND 322[All Fields]) OR (bw57[All Fields] AND 322[All Fields]) OR (bw[All Fields] AND 57322[All Fields]) OR "imunen"[All Fields] OR "imurane"[All Fields] OR "imurek"[All Fields] OR "imuren"[All Fields] OR (nsc[All Fields] AND 39084[All Fields]) OR "thioprine"[All Fields] OR "imidazole"[All Fields] OR "nitroimidazole"[All Fields]) OR "Azathioprine"[Mesh])) OR (("thiopurine*"[All Fields] OR "thioguanin*"[All Fields] OR "2 amino 6 purinethiol"[All Fields] OR "2 amino-6-purinethiol"[All Fields] OR "tabloid"[All Fields] OR "6 thioguanin*"[All Fields] OR "lanvis"[All Fields] OR "2 amino-6-mercaptopurine"[All Fields] OR (2[All Fields] AND amino[All Fields] AND ("purine"[Supplementary Concept] OR "purine"[All Fields] OR "purines"[MeSH Terms] OR "purines"[All Fields]) AND 6[All Fields] AND ("sulfhydryl compounds"[MeSH Terms] OR ("sulfhydryl"[All Fields] AND "compounds"[All Fields]) OR "sulfhydryl compounds"[All Fields] OR "thiol"[All Fields])) OR "2 aminopurine 6 thiol"[All Fields] OR "6 mercaptoguanine"[All Fields] OR "6 thioguanine"[All Fields] OR "nsc 752"[All Fields] OR "thioguanidine"[All Fields] OR "Thioguanine"[Mesh])) OR (("6-mercaptopurine"[All Fields] OR "6-mercaptopurine"[All Fields] OR "6 mercapto purine"[All Fields] OR "6 mercaptopurin"[All Fields] OR (6[All Fields] AND mercaptopurin[All Fields] AND monohydrate[All Fields]) OR "mercaptopurin"[All Fields] OR "thiopurine*"[All Fields] OR "6-thiopurine"[All Fields] OR "6 thiopurine"[All Fields] OR "leupurin"[All Fields] OR ("6-mercaptopurine"[MeSH Terms] OR "6-mercaptopurine"[All Fields]) OR "bw 57 323h"[All Fields] OR "6 thiohypoxanthine"[All Fields] OR "6-thiohypoxanthine"[All Fields] OR (monohydrate[All Fields] AND ("6-mercaptopurine"[MeSH Terms] OR "6-mercaptopurine"[All Fields] OR ("puri"[All Fields] AND "nethol"[All Fields]) OR "puri nethol"[All Fields])) OR "puri-nethol"[All Fields] OR "purinethol"[All Fields] OR "bw 57-323h"[All Fields] OR ((17[All Fields] AND dihydro[All Fields] AND 6h[All Fields] AND ("purine"[Supplementary Concept] OR "purine"[All Fields] OR "purines"[MeSH Terms] OR "purines"[All Fields]) AND 6[All Fields] AND ("thiones"[MeSH Terms] OR "thiones"[All Fields] OR "thione"[All Fields])) AND ("6-mercaptopurine"[MeSH Terms] OR "6-mercaptopurine"[All Fields] OR "mercaptopurine"[All Fields])) OR "6 mp"[All Fields] OR "6mp"[All Fields] OR "6 purinethiol"[All Fields] OR (("6-mercaptopurine"[MeSH Terms] OR "6-mercaptopurine"[All Fields] OR "6 purinethiol"[All Fields]) AND ("dimenhydrinate"[MeSH Terms] OR "dimenhydrinate"[All Fields] OR "hydrate"[All Fields])) OR "classen"[All Fields] OR "e purine"[All Fields] OR "leukeran"[All Fields] OR "lulla"[All Fields] OR "mercaleukin"[All Fields] OR "mercaptene"[All Fields] OR "mern"[All Fields] OR	721

	<p>"mycetine"[All Fields] OR "nsc 755"[All Fields] OR "purine 6 thiol"[All Fields] OR ("purine"[Supplementary Concept] OR "purine"[All Fields] OR "purines"[MeSH Terms] OR "purines"[All Fields]) AND ("sulfhydryl compounds"[MeSH Terms] OR ("sulfhydryl"[All Fields] AND "compounds"[All Fields]) OR "sulfhydryl compounds"[All Fields] OR "thiol"[All Fields]) AND 6[All Fields] OR "purinethiol"[All Fields] OR "thiohypoxanthine"[All Fields] OR "paludrine"[All Fields] OR "6-Mercaptopurine"[Mesh:noexp])) AND (((("hplc" OR "high pressure liquid chromatography" OR "cytologic* techniq*" OR "cytologic* technic*" OR "hematolog* (test OR tests OR testing)" OR "haematolog* (test OR tests OR testing)" OR "blood (test OR tests OR testing)" OR "radioassay" OR "radioreceptor" OR "radioligand*") OR (((((((((((((((("Phenotype"[Mesh])) OR "Chemistry Techniques, Analytical"[Mesh:NoExp])) OR "Chromatography"[Mesh:NoExp]) OR "Chromatography, Liquid"[Mesh:NoExp]) OR "Chromatography, High Pressure Liquid"[Mesh]) OR "Investigative Techniques"[Mesh:NoExp]) OR "Enzyme Assays"[Mesh]) OR "Clinical Enzyme Tests"[Mesh]) OR "Clinical Chemistry Tests"[Mesh:NoExp]) OR "Blood Chemical Analysis"[Mesh:NoExp]) OR "Cytological Techniques"[Mesh]) OR "Hematologic Tests"[Mesh]) OR "Radioligand Assay"[Mesh]) OR "Mass Spectrometry"[Mesh:NoExp]) OR "Tandem Mass Spectrometry"[Mesh])))) OR (((("genotype" OR "microchip" OR "pharmacogen*" OR "toxicogenetic*" OR "(genotyp* OR genetic*) AND (test OR tests OR testing OR screen*)" OR "(genetic* OR genotyp*) AND (predispose OR predisposition OR predisposal)" OR "biomarker" OR "PCR")) OR (((((((((((((((((((("Genotype"[Mesh:NoExp]) OR "Genetic Predisposition to Disease"[Mesh]) OR "Hemizygote"[Mesh]) OR "Heterozygote"[Mesh]) OR "Homozygote"[Mesh]) OR "Genetic Markers"[Mesh]) OR "Biomarkers, Pharmacological"[Mesh]) OR "Biological Markers"[Mesh:NoExp]) OR "Genetic Techniques"[Mesh:NoExp]) OR "Chromosome Mapping"[Mesh]) OR "Cytogenetic Analysis"[Mesh]) OR "Microchip Analytical Procedures"[Mesh]) OR "Microarray Analysis"[Mesh]) OR "Oligonucleotide Array Sequence Analysis"[Mesh]) OR "Sequence Analysis"[Mesh]) OR "Genome-Wide Association Study"[Mesh]) OR "Genetic Association Studies"[Mesh]) OR "Gene Expression Profiling"[Mesh]) OR "Genetic Testing"[Mesh]) OR "Molecular Diagnostic Techniques"[Mesh:NoExp]) OR "Genotyping Techniques"[Mesh]) OR "Heterozygote Detection"[Mesh]) OR "Nucleic Acid Amplification Techniques"[Mesh]) OR "Ligase Chain Reaction"[Mesh]) OR "Polymerase Chain Reaction"[Mesh]) OR "Self-Sustained Sequence Replication"[Mesh]) OR "Nucleic Acid Denaturation"[Mesh]) OR "Restriction Mapping"[Mesh]) OR "DNA Fingerprinting"[Mesh]) OR "Amplified Fragment Length Polymorphism Analysis"[Mesh]) OR "Pharmacogenetics"[Mesh]) OR "Toxicogenetics"[Mesh]) OR "Genetics"[Mesh:NoExp]) OR "Genetic Research"[Mesh:NoExp]) OR "Genetics, Medical"[Mesh]) OR "Genetics, Population"[Mesh:NoExp]) OR "Genomics"[Mesh]))))</p>	
#258	<p>Search (((("hplc" OR "high pressure liquid chromatography" OR "cytologic* techniq*" OR "cytologic* technic*" OR "hematolog* (test OR tests OR testing)" OR "haematolog* (test OR tests OR testing)" OR "blood (test OR tests OR testing)" OR "radioassay" OR "radioreceptor" OR "radioligand*") OR (((((((((((((((("Phenotype"[Mesh])) OR "Chemistry Techniques, Analytical"[Mesh:NoExp])) OR "Chromatography"[Mesh:NoExp]) OR "Chromatography, Liquid"[Mesh:NoExp]) OR "Chromatography, High Pressure Liquid"[Mesh]) OR "Investigative Techniques"[Mesh:NoExp]) OR "Enzyme Assays"[Mesh]) OR "Clinical Enzyme Tests"[Mesh]) OR "Clinical Chemistry Tests"[Mesh:NoExp]) OR "Blood Chemical Analysis"[Mesh:NoExp]) OR "Cytological Techniques"[Mesh]) OR "Hematologic Tests"[Mesh]) OR "Radioligand Assay"[Mesh]) OR "Mass Spectrometry"[Mesh:NoExp]) OR "Tandem Mass Spectrometry"[Mesh])))) OR (((("genotype" OR "microchip" OR "pharmacogen*" OR "toxicogenetic*" OR "(genotyp* OR genetic*) AND (test OR tests OR testing OR screen*)" OR "(genetic* OR genotyp*) AND (predispose OR predisposition OR predisposal)" OR "biomarker" OR "PCR")) OR (((((((((((((((((((("Genotype"[Mesh:NoExp]) OR "Genetic Predisposition to Disease"[Mesh]) OR "Hemizygote"[Mesh]) OR "Heterozygote"[Mesh]) OR "Homozygote"[Mesh]) OR "Genetic Markers"[Mesh]) OR "Biomarkers, Pharmacological"[Mesh]) OR "Biological Markers"[Mesh:NoExp]) OR "Genetic Techniques"[Mesh:NoExp]) OR "Chromosome Mapping"[Mesh]) OR "Cytogenetic Analysis"[Mesh]) OR "Microchip Analytical Procedures"[Mesh]) OR "Microarray Analysis"[Mesh]) OR "Oligonucleotide Array Sequence Analysis"[Mesh]) OR "Sequence Analysis"[Mesh]) OR "Genome-Wide Association Study"[Mesh]) OR "Genetic Association Studies"[Mesh]) OR "Gene Expression Profiling"[Mesh]) OR "Genetic Testing"[Mesh]) OR "Molecular Diagnostic Techniques"[Mesh:NoExp]) OR "Genotyping Techniques"[Mesh]) OR "Heterozygote Detection"[Mesh]) OR "Nucleic Acid Amplification Techniques"[Mesh]) OR "Ligase Chain Reaction"[Mesh]) OR "Polymerase Chain Reaction"[Mesh]) OR "Self-Sustained Sequence Replication"[Mesh]) OR "Nucleic Acid Denaturation"[Mesh]) OR "Restriction Mapping"[Mesh]) OR "DNA Fingerprinting"[Mesh]) OR "Amplified Fragment Length Polymorphism Analysis"[Mesh]) OR "Pharmacogenetics"[Mesh]) OR "Toxicogenetics"[Mesh]) OR "Genetics"[Mesh:NoExp]) OR "Genetic Research"[Mesh:NoExp]) OR "Genetics, Medical"[Mesh]) OR "Genetics, Population"[Mesh:NoExp]) OR "Genomics"[Mesh]))))</p>	2933066

	<p>screen*)" OR "(genetic* OR genotyp*) AND (predispose OR predisposition OR predisposal)" OR "biomarker" OR "PCR")) OR ((("Genotype"[Mesh:NoExp]) OR "Genetic Predisposition to Disease"[Mesh]) OR "Hemizygote"[Mesh]) OR "Heterozygote"[Mesh]) OR "Homozygote"[Mesh]) OR "Genetic Markers"[Mesh]) OR "Biomarkers, Pharmacological"[Mesh]) OR "Biological Markers"[Mesh:NoExp]) OR "Genetic Techniques"[Mesh:NoExp]) OR "Chromosome Mapping"[Mesh]) OR "Cytogenetic Analysis"[Mesh]) OR "Microchip Analytical Procedures"[Mesh]) OR "Microarray Analysis"[Mesh]) OR "Oligonucleotide Array Sequence Analysis"[Mesh]) OR "Sequence Analysis"[Mesh]) OR "Genome-Wide Association Study"[Mesh]) OR "Genetic Association Studies"[Mesh]) OR "Gene Expression Profiling"[Mesh]) OR "Genetic Testing"[Mesh]) OR "Molecular Diagnostic Techniques"[Mesh:NoExp]) OR "Genotyping Techniques"[Mesh]) OR "Heterozygote Detection"[Mesh]) OR "Nucleic Acid Amplification Techniques"[Mesh]) OR "Ligase Chain Reaction"[Mesh]) OR "Polymerase Chain Reaction"[Mesh]) OR "Self-Sustained Sequence Replication"[Mesh]) OR "Nucleic Acid Denaturation"[Mesh]) OR "Restriction Mapping"[Mesh]) OR "DNA Fingerprinting"[Mesh]) OR "Amplified Fragment Length Polymorphism Analysis"[Mesh]) OR "Pharmacogenetics"[Mesh]) OR "Toxicogenetics"[Mesh]) OR "Genetics"[Mesh:NoExp]) OR "Genetic Research"[Mesh:NoExp]) OR "Genetics, Medical"[Mesh]) OR "Genetics, Population"[Mesh:NoExp]) OR "Genomics"[Mesh]))</p>	
#257	<p>Search (("hplc" OR "high pressure liquid chromatography" OR "cytologic* techniq*" OR "cytologic* technic*" OR "hematolog* (test OR tests OR testing)" OR "haematolog* (test OR tests OR testing)" OR "blood (test OR tests OR testing)" OR "radioassay" OR "radioreceptor" OR "radioligand*")) OR ((("Phenotype"[Mesh])) OR "Chemistry Techniques, Analytical"[Mesh:NoExp])) OR "Chromatography"[Mesh:NoExp]) OR "Chromatography, Liquid"[Mesh:NoExp]) OR "Chromatography, High Pressure Liquid"[Mesh]) OR "Investigative Techniques"[Mesh:NoExp]) OR "Enzyme Assays"[Mesh]) OR "Clinical Enzyme Tests"[Mesh]) OR "Clinical Chemistry Tests"[Mesh:NoExp]) OR "Blood Chemical Analysis"[Mesh:NoExp]) OR "Cytological Techniques"[Mesh]) OR "Hematologic Tests"[Mesh]) OR "Radioligand Assay"[Mesh]) OR "Mass Spectrometry"[Mesh:NoExp]) OR "Tandem Mass Spectrometry"[Mesh]))</p>	1867338
#256	<p>Search (("genotype" OR "microchip" OR "pharmacogen*" OR "toxicogenetic*" OR "(genotyp* OR genetic*) AND (test OR tests OR testing OR screen*)" OR "(genetic* OR genotyp*) AND (predispose OR predisposition OR predisposal)" OR "biomarker" OR "PCR")) OR (("Genotype"[Mesh:NoExp]) OR "Genetic Predisposition to Disease"[Mesh]) OR "Hemizygote"[Mesh]) OR "Heterozygote"[Mesh]) OR "Homozygote"[Mesh]) OR "Genetic Markers"[Mesh]) OR "Biomarkers, Pharmacological"[Mesh]) OR "Biological Markers"[Mesh:NoExp]) OR "Genetic Techniques"[Mesh:NoExp]) OR "Chromosome Mapping"[Mesh]) OR "Cytogenetic Analysis"[Mesh]) OR "Microchip Analytical Procedures"[Mesh]) OR "Microarray Analysis"[Mesh]) OR "Oligonucleotide Array Sequence Analysis"[Mesh]) OR "Sequence Analysis"[Mesh]) OR "Genome-Wide Association Study"[Mesh]) OR "Genetic Association Studies"[Mesh]) OR "Gene Expression Profiling"[Mesh]) OR "Genetic Testing"[Mesh]) OR "Molecular Diagnostic Techniques"[Mesh:NoExp]) OR "Genotyping Techniques"[Mesh]) OR "Heterozygote Detection"[Mesh]) OR "Nucleic Acid Amplification Techniques"[Mesh]) OR "Ligase Chain Reaction"[Mesh]) OR "Polymerase Chain Reaction"[Mesh]) OR "Self-Sustained Sequence Replication"[Mesh]) OR "Nucleic Acid Denaturation"[Mesh]) OR "Restriction Mapping"[Mesh]) OR "DNA Fingerprinting"[Mesh]) OR "Amplified Fragment Length Polymorphism Analysis"[Mesh]) OR "Pharmacogenetics"[Mesh]) OR "Toxicogenetics"[Mesh]) OR "Genetics"[Mesh:NoExp]) OR "Genetic Research"[Mesh:NoExp]) OR "Genetics, Medical"[Mesh]) OR "Genetics,</p>	1427650

	Population"[Mesh:NoExp]) OR "Genomics"[Mesh])	
#255	Search (((("Methyltransferases"[Mesh] OR ("thiopurine methyltransferase"[Supplementary Concept] OR "Thiopurine S methyltransferase deficiency"[Supplementary Concept])) OR ("thiopurine methyltransferase"[All Fields] OR "thiopurine s methyltransferase"[All Fields] OR "thiopurine s-methyltransferase"[All Fields] OR (e.c.[All Fields] AND 2.1.1.67[All Fields]) OR "ec 2.1.1.67"[All Fields] OR "tpmt"[All Fields]))) AND (((("azothioprine"[All Fields] OR "imurel"[All Fields] OR "imuran"[All Fields] OR "immuran"[All Fields] OR "azathioprine"[All Fields] OR "thiopurine*"[All Fields] OR "6 (1 methyl 4 nitro 5 imidazolyl) mercaptopurine"[All Fields] OR (aza[All Fields] AND q[All Fields]) OR "azamun*"[All Fields] OR "azaprine"[All Fields] OR "ahasan"[All Fields] OR (azathio[All Fields] AND dura[All Fields]) OR "azathioprine"[All Fields] OR "azathiopurine"[All Fields] OR "azatrux"[All Fields] OR "azatrinem"[All Fields] OR "azodi"[All Fields] OR "azorean"[All Fields] OR (bw[All Fields] AND 57[All Fields] AND 322[All Fields]) OR (bw57[All Fields] AND 322[All Fields]) OR (bw[All Fields] AND 57322[All Fields]) OR "imunen"[All Fields] OR "imurane"[All Fields] OR "imurek"[All Fields] OR "imuren"[All Fields] OR (nsc[All Fields] AND 39084[All Fields]) OR "thioprine"[All Fields] OR "imidazole"[All Fields] OR "nitroimidazole"[All Fields]) OR "Azathioprine"[Mesh])) OR ("thiopurine*"[All Fields] OR "thioguanin*"[All Fields] OR "2 amino 6 purinethiol"[All Fields] OR "2 amino-6-purinethiol"[All Fields] OR "tabloid"[All Fields] OR "6 thioguanin*"[All Fields] OR "lanvis"[All Fields] OR "2 amino-6-mercaptopurine"[All Fields] OR (2[All Fields] AND amino[All Fields] AND ("purine"[Supplementary Concept] OR "purine"[All Fields] OR "purines"[MeSH Terms] OR "purines"[All Fields]) AND 6[All Fields] AND ("sulfhydryl compounds"[MeSH Terms] OR ("sulfhydryl"[All Fields] AND "compounds"[All Fields]) OR "sulfhydryl compounds"[All Fields] OR "thiol"[All Fields])) OR "2 aminopurine 6 thiol"[All Fields] OR "6 mercaptoguanine"[All Fields] OR "6 thioquanine"[All Fields] OR "nsc 752"[All Fields] OR "thioguanidine"[All Fields]) OR "Thioguanine"[Mesh])) OR (("6-mercaptopurine"[All Fields] OR "6-mercaptopurine"[All Fields] OR "6 mercapto purine"[All Fields] OR "6 mercaptopurin"[All Fields] OR (6[All Fields] AND mercaptopurin[All Fields] AND monohydrate[All Fields]) OR "mercaptopurin"[All Fields] OR "thiopurine*"[All Fields] OR "6-thiopurine"[All Fields] OR "6 thiopurine"[All Fields] OR "leupurin"[All Fields] OR ("6-mercaptopurine"[MeSH Terms] OR "6-mercaptopurine"[All Fields]) OR "bw 57 323h"[All Fields] OR "6 thiohypoxanthine"[All Fields] OR "6-thiohypoxanthine"[All Fields] OR (monohydrate[All Fields] AND ("6-mercaptopurine"[MeSH Terms] OR "6-mercaptopurine"[All Fields] OR ("puri"[All Fields] AND "nethol"[All Fields]) OR "puri nethol"[All Fields])) OR "puri-nethol"[All Fields] OR "purinethol"[All Fields] OR "bw 57-323h"[All Fields] OR ((17[All Fields] AND dihydro[All Fields] AND 6h[All Fields] AND ("purine"[Supplementary Concept] OR "purine"[All Fields] OR "purines"[MeSH Terms] OR "purines"[All Fields]) AND 6[All Fields] AND ("thiones"[MeSH Terms] OR "thiones"[All Fields] OR "thione"[All Fields])) AND ("6-mercaptopurine"[MeSH Terms] OR "6-mercaptopurine"[All Fields] OR "mercaptopurine"[All Fields])) OR "6 mp"[All Fields] OR "6mp"[All Fields] OR "6 purinethiol"[All Fields] OR (("6-mercaptopurine"[MeSH Terms] OR "6-mercaptopurine"[All Fields] OR "6 purinethiol"[All Fields]) AND ("dimenhydrinate"[MeSH Terms] OR "dimenhydrinate"[All Fields] OR "hydrate"[All Fields])) OR "classen"[All Fields] OR "e purine"[All Fields] OR "leukeran"[All Fields] OR "lulla"[All Fields] OR "mercaleukin"[All Fields] OR "mercaptene"[All Fields] OR "mern"[All Fields] OR "mycetine"[All Fields] OR "nsc 755"[All Fields] OR "purine 6 thiol"[All Fields] OR ("purine"[Supplementary Concept] OR "purine"[All Fields] OR "purines"[MeSH Terms] OR "purines"[All Fields]) AND ("sulfhydryl compounds"[MeSH Terms] OR ("sulfhydryl"[All Fields] AND "compounds"[All Fields]) OR "sulfhydryl compounds"[All Fields] OR "thiol"[All Fields]) AND 6[All Fields]) OR "purinethiol"[All Fields] OR "thiohypoxanthine"[All Fields] OR "paludrine"[All Fields] OR "6-	1192

	Mercaptopurine"[Mesh:noexp]))	
#254	Search (((("azothioprine"[All Fields] OR "imurel"[All Fields] OR "imuran"[All Fields] OR "immuran"[All Fields] OR "azathioprine"[All Fields] OR "thiopurine*"[All Fields] OR "6 (1 methyl 4 nitro 5 imidazolyl) mercaptopurine"[All Fields] OR (aza[All Fields] AND q[All Fields]) OR "azamun*"[All Fields] OR "azaprine"[All Fields] OR "ahasan"[All Fields] OR (azathio[All Fields] AND dura[All Fields]) OR "azathioprine"[All Fields] OR "azathiopurine"[All Fields] OR "azatrux"[All Fields] OR "azatrinem"[All Fields] OR "azodi"[All Fields] OR "azorean"[All Fields] OR (bw[All Fields] AND 57[All Fields] AND 322[All Fields]) OR (bw57[All Fields] AND 322[All Fields]) OR (bw[All Fields] AND 57322[All Fields]) OR "imunen"[All Fields] OR "imurane"[All Fields] OR "imurek"[All Fields] OR "imuren"[All Fields] OR (nsc[All Fields] AND 39084[All Fields]) OR "thioprine"[All Fields] OR "imidazole"[All Fields] OR "nitroimidazole"[All Fields] OR "Azathioprine"[Mesh])) OR (("thiopurine*"[All Fields] OR "thioguanin*"[All Fields] OR "2 amino 6 purinethiol"[All Fields] OR "2 amino-6-purinethiol"[All Fields] OR "tabloid"[All Fields] OR "6 thioguanin*"[All Fields] OR "lanvis"[All Fields] OR "2 amino-6-mercaptopurine"[All Fields] OR (2[All Fields] AND amino[All Fields] AND ("purine"[Supplementary Concept] OR "purine"[All Fields] OR "purines"[MeSH Terms] OR "purines"[All Fields]) AND 6[All Fields] AND ("sulfhydryl compounds"[MeSH Terms] OR ("sulfhydryl"[All Fields] AND "compounds"[All Fields]) OR "sulfhydryl compounds"[All Fields] OR "thiol"[All Fields])) OR "2 aminopurine 6 thiol"[All Fields] OR "6 mercaptoguanine"[All Fields] OR "6 thioquanine"[All Fields] OR "nsc 752"[All Fields] OR "thioguanidine"[All Fields] OR "Thioguanine"[Mesh])) OR (("6-mercaptopurine"[All Fields] OR "6-mercaptopurine"[All Fields] OR "6 mercapto purine"[All Fields] OR "6 mercaptopurin"[All Fields] OR (6[All Fields] AND mercaptopurin[All Fields] AND monohydrate[All Fields]) OR "mercaptopurin"[All Fields] OR "thiopurine*"[All Fields] OR "6-thiopurine"[All Fields] OR "6 thiopurine"[All Fields] OR "leupurin"[All Fields] OR ("6-mercaptopurine"[MeSH Terms] OR "6-mercaptopurine"[All Fields]) OR "bw 57 323h"[All Fields] OR "6 thiohypoxanthine"[All Fields] OR "6-thiohypoxanthine"[All Fields] OR (monohydrate[All Fields] AND ("6-mercaptopurine"[MeSH Terms] OR "6-mercaptopurine"[All Fields] OR ("puri"[All Fields] AND "nethol"[All Fields]) OR "puri nethol"[All Fields])) OR "puri-nethol"[All Fields] OR "purinethol"[All Fields] OR "bw 57-323h"[All Fields] OR ((17[All Fields] AND dihydro[All Fields] AND 6h[All Fields] AND ("purine"[Supplementary Concept] OR "purine"[All Fields] OR "purines"[MeSH Terms] OR "purines"[All Fields]) AND 6[All Fields] AND ("thiones"[MeSH Terms] OR "thiones"[All Fields] OR "thione"[All Fields])) AND ("6-mercaptopurine"[MeSH Terms] OR "6-mercaptopurine"[All Fields] OR "mercaptopurine"[All Fields])) OR "6 mp"[All Fields] OR "6mp"[All Fields] OR "6 purinethiol"[All Fields] OR (("6-mercaptopurine"[MeSH Terms] OR "6-mercaptopurine"[All Fields] OR "6 purinethiol"[All Fields]) AND ("dimenhydrinate"[MeSH Terms] OR "dimenhydrinate"[All Fields] OR "hydrate"[All Fields])) OR "classen"[All Fields] OR "e purine"[All Fields] OR "leukeran"[All Fields] OR "lulla"[All Fields] OR "mercaleukin"[All Fields] OR "mercaptene"[All Fields] OR "mern"[All Fields] OR "mycetine"[All Fields] OR "nsc 755"[All Fields] OR "purine 6 thiol"[All Fields] OR (("purine"[Supplementary Concept] OR "purine"[All Fields] OR "purines"[MeSH Terms] OR "purines"[All Fields]) AND ("sulfhydryl compounds"[MeSH Terms] OR ("sulfhydryl"[All Fields] AND "compounds"[All Fields]) OR "sulfhydryl compounds"[All Fields] OR "thiol"[All Fields]) AND 6[All Fields]) OR "purinethiol"[All Fields] OR "thiohypoxanthine"[All Fields] OR "paludrine"[All Fields]) OR "6-Mercaptopurine"[Mesh:noexp]))	48157
#253	Search "genotype" OR "microchip" OR "pharmacogen*" OR "toxicogenetic*" OR "(genotyp* OR genetic*) AND (test OR tests OR testing OR screen*)" OR "(genetic* OR genotyp*) AND (predispose OR predisposition OR predisposal)" OR "biomarker" OR "PCR"	554199

#252	Search (((((((((((((((((((((((((((((((("Genotype"[Mesh:NoExp]) OR "Genetic Predisposition to Disease"[Mesh]) OR "Hemizygote"[Mesh]) OR "Heterozygote"[Mesh]) OR "Homozygote"[Mesh]) OR "Genetic Markers"[Mesh]) OR "Biomarkers, Pharmacological"[Mesh]) OR "Biological Markers"[Mesh:NoExp]) OR "Genetic Techniques"[Mesh:NoExp]) OR "Chromosome Mapping"[Mesh]) OR "Cytogenetic Analysis"[Mesh]) OR "Microchip Analytical Procedures"[Mesh]) OR "Microarray Analysis"[Mesh]) OR "Oligonucleotide Array Sequence Analysis"[Mesh]) OR "Sequence Analysis"[Mesh]) OR "Genome-Wide Association Study"[Mesh]) OR "Genetic Association Studies"[Mesh]) OR "Gene Expression Profiling"[Mesh]) OR "Genetic Testing"[Mesh]) OR "Molecular Diagnostic Techniques"[Mesh:NoExp]) OR "Genotyping Techniques"[Mesh]) OR "Heterozygote Detection"[Mesh]) OR "Nucleic Acid Amplification Techniques"[Mesh]) OR "Ligase Chain Reaction"[Mesh]) OR "Polymerase Chain Reaction"[Mesh]) OR "Self-Sustained Sequence Replication"[Mesh]) OR "Nucleic Acid Denaturation"[Mesh]) OR "Restriction Mapping"[Mesh]) OR "DNA Fingerprinting"[Mesh]) OR "Amplified Fragment Length Polymorphism Analysis"[Mesh]) OR "Pharmacogenetics"[Mesh]) OR "Toxicogenetics"[Mesh]) OR "Genetics"[Mesh:NoExp]) OR "Genetic Research"[Mesh:NoExp]) OR "Genetics, Medical"[Mesh]) OR "Genetics, Population"[Mesh:NoExp]) OR "Genomics"[Mesh]	1238457
#251	Search "hplc" OR "high pressure liquid chromatography" OR "cytologic* techniq*" OR "cytologic* technic*" OR "hematolog* (test OR tests OR testing)" OR "haematolog* (test OR tests OR testing)" OR "blood (test OR tests OR testing)" OR "radioassay" OR "radioreceptor" OR "radioligand*"	250449
#250	Search (((((((((((((((("Phenotype"[Mesh])) OR "Chemistry Techniques, Analytical"[Mesh:NoExp])) OR "Chromatography"[Mesh:NoExp]) OR "Chromatography, Liquid"[Mesh:NoExp]) OR "Chromatography, High Pressure Liquid"[Mesh]) OR "Investigative Techniques"[Mesh:NoExp]) OR "Enzyme Assays"[Mesh]) OR "Clinical Enzyme Tests"[Mesh]) OR "Clinical Chemistry Tests"[Mesh:NoExp]) OR "Blood Chemical Analysis"[Mesh:NoExp]) OR "Cytological Techniques"[Mesh]) OR "Hematologic Tests"[Mesh]) OR "Radioligand Assay"[Mesh]) OR "Mass Spectrometry"[Mesh:NoExp]) OR "Tandem Mass Spectrometry"[Mesh]	1807379
#249	Search ("Methyltransferases"[Mesh] OR ("thiopurine methyltransferase"[Supplementary Concept] OR "Thiopurine S methyltransferase deficiency"[Supplementary Concept])) OR ("thiopurine methyltransferase"[All Fields] OR "thiopurine s methyltransferase"[All Fields] OR "thiopurine s-methyltransferase"[All Fields] OR (e.c.[All Fields] AND 2.1.1.67[All Fields]) OR "ec 2.1.1.67"[All Fields] OR "tpmt"[All Fields])	31423
#248	Search ("6-mercaptapurine"[All Fields] OR "6-mercaptapurine"[All Fields] OR "6 mercapto purine"[All Fields] OR "6 mercaptapurin"[All Fields] OR (6[All Fields] AND mercaptapurin[All Fields] AND monohydrate[All Fields]) OR "mercaptapurin"[All Fields] OR "thiopurine*" [All Fields] OR "6-thiopurine"[All Fields] OR "6 thiopurine"[All Fields] OR "leupurin"[All Fields] OR ("6-mercaptapurine"[MeSH Terms] OR "6-mercaptapurine"[All Fields]) OR "bw 57 323h"[All Fields] OR "6 thiohypoxanthine"[All Fields] OR "6-thiohypoxanthine"[All Fields] OR (monohydrate[All Fields] AND ("6-mercaptapurine"[MeSH Terms] OR "6-mercaptapurine"[All Fields] OR ("puri"[All Fields] AND "nethol"[All Fields]) OR "puri nethol"[All Fields])) OR "puri-nethol"[All Fields] OR "purinethol"[All Fields] OR "bw 57-323h"[All Fields] OR ((17[All Fields] AND dihydro[All Fields] AND 6h[All Fields] AND ("purine"[Supplementary Concept] OR "purine"[All Fields] OR "purines"[MeSH Terms] OR "purines"[All Fields]) AND 6[All Fields] AND ("thiones"[MeSH Terms] OR "thiones"[All Fields] OR "thione"[All Fields])) AND ("6-mercaptapurine"[MeSH Terms] OR "6-mercaptapurine"[All Fields] OR "mercaptapurine"[All Fields])) OR "6	23146

	mp"[All Fields] OR "6mp"[All Fields] OR "6 purinethiol"[All Fields] OR (("6-mercaptapurine"[MeSH Terms] OR "6-mercaptapurine"[All Fields] OR "6 purinethiol"[All Fields]) AND ("dimenhydrinate"[MeSH Terms] OR "dimenhydrinate"[All Fields] OR "hydrate"[All Fields])) OR "classen"[All Fields] OR "e purine"[All Fields] OR "leukeran"[All Fields] OR "lulla"[All Fields] OR "mercaleukin"[All Fields] OR "mercaptene"[All Fields] OR "mern"[All Fields] OR "mycetine"[All Fields] OR "nsc 755"[All Fields] OR "purine 6 thiol"[All Fields] OR (("purine"[Supplementary Concept] OR "purine"[All Fields] OR "purines"[MeSH Terms] OR "purines"[All Fields]) AND ("sulfhydryl compounds"[MeSH Terms] OR "sulfhydryl"[All Fields] AND "compounds"[All Fields]) OR "sulfhydryl compounds"[All Fields] OR "thiol"[All Fields]) AND 6[All Fields]) OR "purinethiol"[All Fields] OR "thiohypoxanthine"[All Fields] OR "paludrine"[All Fields]) OR "6-Mercaptapurine"[Mesh:noexp]	
#247	Search ("thiopurine*" [All Fields] OR "thioguanin*" [All Fields] OR "2 amino 6 purinethiol"[All Fields] OR "2 amino-6-purinethiol"[All Fields] OR "tabloid"[All Fields] OR "6 thioguanin*" [All Fields] OR "lanvis"[All Fields] OR "2 amino-6-mercaptapurine"[All Fields] OR (2[All Fields] AND amino[All Fields] AND ("purine"[Supplementary Concept] OR "purine"[All Fields] OR "purines"[MeSH Terms] OR "purines"[All Fields]) AND 6[All Fields] AND ("sulfhydryl compounds"[MeSH Terms] OR ("sulfhydryl"[All Fields] AND "compounds"[All Fields]) OR "sulfhydryl compounds"[All Fields] OR "thiol"[All Fields])) OR "2 aminopurine 6 thiol"[All Fields] OR "6 mercaptoguanine"[All Fields] OR "6 thioquanine"[All Fields] OR "nsc 752"[All Fields] OR "thioguanidine"[All Fields]) OR "Thioguanine"[Mesh]	4090
#246	Search "thiopurine*" OR "thioguanin*" OR "2 amino 6 purinethiol" OR "2 amino-6-purinethiol" OR "tabloid" OR "6 thioguanin*" OR "lanvis" OR "2 amino-6-mercaptapurine" OR "2 amino purine 6 thiol" OR "2 aminopurine 6 thiol" OR "6 mercaptoguanine" OR "6 thioquanine" OR "nsc 752" OR "thioguanidine"	1981
#245	Search ("azothioprine"[All Fields] OR "imurel"[All Fields] OR "imuran"[All Fields] OR "immuran"[All Fields] OR "azathioprine"[All Fields] OR "thiopurine*" [All Fields] OR "6 (1 methyl 4 nitro 5 imidazolyl) mercaptapurine"[All Fields] OR (aza[All Fields] AND q[All Fields]) OR "azamun*" [All Fields] OR "azaprine"[All Fields] OR "ahasan"[All Fields] OR "azathio[All Fields] AND dura[All Fields]) OR "azathioprine"[All Fields] OR "azathiopurine"[All Fields] OR "azatruX"[All Fields] OR "azatrinem"[All Fields] OR "azodi"[All Fields] OR "azorean"[All Fields] OR (bw[All Fields] AND 57[All Fields] AND 322[All Fields]) OR (bw57[All Fields] AND 322[All Fields]) OR (bw[All Fields] AND 57322[All Fields]) OR "imunen"[All Fields] OR "imurane"[All Fields] OR "imurek"[All Fields] OR "imuren"[All Fields] OR (nsc[All Fields] AND 39084[All Fields]) OR "thioprine"[All Fields] OR "imidazole"[All Fields] OR "nitroimidazole"[All Fields]) OR "Azathioprine"[Mesh]	37578
#244	Search (("azothioprine" OR "imurel" OR "imuran" OR "immuran" OR "azathioprine" OR "thiopurine*" OR "6 (1 methyl 4 nitro 5 imidazolyl) mercaptapurine" OR "aza-q" OR "azamun*" OR "azaprine" OR "ahasan" OR "azathio dura" OR "azathioprine" OR "azathiopurine" OR "azatruX" OR "azatrinem" OR "azodi" OR "azorean" OR "bw 57 322" OR "bw57-322" OR "bw 57322" OR "imunen" OR "imurane" OR "imurek" OR "imuren" OR "nsc 39084" OR "thioprine" OR "imidazole" OR "nitroimidazole")) OR "azathioprine"[Mesh]	37578
#243	Search "azothioprine" OR "imurel" OR "imuran" OR "immuran" OR "azathioprine" OR "thiopurine*" OR "6 (1 methyl 4 nitro 5 imidazolyl) mercaptapurine" OR "aza-q" OR "azamun*" OR "azaprine" OR "ahasan" OR "azathio dura" OR "azathioprine" OR "azathiopurine" OR "azatruX" OR "azatrinem" OR "azodi" OR "azorean" OR "bw 57 322" OR "bw57-322" OR "bw 57322" OR "imunen" OR "imurane" OR "imurek" OR "imuren" OR "nsc 39084" OR "thioprine" OR "imidazole" OR "nitroimidazole"	37578

#242	<p>Search ("azothioprine"[All Fields] OR "imurel"[All Fields] OR "imuran"[All Fields] OR "immuran"[All Fields] OR "azathioprine"[All Fields] OR "thiopurine*"[All Fields] OR "6 (1 methyl 4 nitro 5 imidazolyl) mercaptopurine"[All Fields] OR (aza[All Fields] AND q[All Fields]) OR "azamun*"[All Fields] OR "azaprime"[All Fields] OR "ahasan"[All Fields] OR (azathio[All Fields] AND dura[All Fields]) OR "azathioprine"[All Fields] OR "azathiopurine"[All Fields] OR "azatrux"[All Fields] OR "azatrinem"[All Fields] OR "azodi"[All Fields] OR "azorean"[All Fields] OR (bw[All Fields] AND 57[All Fields] AND 322[All Fields]) OR (bw57[All Fields] AND 322[All Fields]) OR (bw[All Fields] AND 57322[All Fields]) OR "imunen"[All Fields] OR "imurane"[All Fields] OR "imurek"[All Fields] OR "imuren"[All Fields] OR (nsc[All Fields] AND 39084[All Fields]) OR "thioprine"[All Fields] OR "imidazole"[All Fields] OR "nitroimidazole"[All Fields]) OR "Azathioprine"[Mesh] Thioguanine)</p>	607
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Appendix B – Grey literature search

Agency Abbreviated Name	Agency, Organization, Website Full Name	Country	URL
ANZHSN	Australia and New Zealand Horizon Scanning Network - Technologies Assessed	Australia	http://www.horizonscanning.gov.au/internet/horizon/publishing.nsf/Content/technologies-assessed-lp-2
MSAC	Australian Government Department of Health and Ageing - Medical Services Advisory Committee	Australia	http://www.msac.gov.au/internet/msac/publishing.nsf/Content/completed-assessments
ASERNIP-S	Australian Safety and Efficacy Register of New Interventional Procedures – Surgical	Australia	http://www.surgeons.org/policies-publications/publications/
CCE	Centre for Clinical Effectiveness	Australia	http://www.southernhealth.org.au/page/Health_Professionals/CCE/Evidence_reviews/
CHERE	Centre for Health Economics Research and Evaluation	Australia	http://datasearch.uts.edu.au/chere/publications/working-papers.cfm http://cfsites1.uts.edu.au/chere/publications/index.cfm?year=2012
	Department of Health and Ageing, Australian Government	Australia	http://www.health.gov.au/internet/main/publishing.nsf/Content/health-publicat.htm
HealthPACT	Health Policy Advisory Committee on Technology, Queensland Government	Australia	http://www.health.qld.gov.au/healthpact/html/tech-evaluated.asp
	Monash Health Centre for Clinical Effectiveness	Australia	http://www.monashhealth.org/page/results
NHSU	National Horizon Scanning Unit	Australia	http://www.horizonscanning.gov.au/internet/horizon/publishing.nsf/Content/horizon-scanning-reports-2
NPS RADAR	National Prescribing Service	Australia	http://www.nps.org.au/publications/health-professional/nps-radar
	NPS Medicine Wise	Australia	http://www.nps.org.au/medicines/cancers/antimetabolites-chemotherapy/mercaptopurine/puri-nethol-tablets
NPS RADAR	NPS RADAR	Australia	http://www.npsradar.org.au/site.php?page=1&content=/npsradar%2Fcontent%2Farchive_alpha.html

	Queensland Government (Australia)	Australia	http://www.health.qld.gov.au/healthpact/html/tech-evaluated.asp
QH	Queensland Health	Australia	http://pan.search.qld.gov.au/search/search.cgi?num_ranks=10&tiers=off&collection=qld-gov&profile=health&query=thiopurine&x=0&y=0
	Royal Australian College of Surgeons	Australia	http://www.surgeons.org/for-health-professionals/audits-and-surgical-research/asernips/systematic-reviews-and-technology-overviews/
CCE	Southern Health-Centre for Clinical Effectiveness	Australia	http://www.southernhealth.org.au/page/Health_Professionals/CCE/
JBI	The Joanna Briggs Institute, The University of Adelaide	Australia	http://ovidsp.ovid.com/
UA	University of Adelaide	Australia	http://joannabriggs.org/about.html
ITA	Institute of Technology Assessment	Austria	http://www.oeaw.ac.at/ita/index.htm
LBI	Ludwig Boltzmann Institut für Health Technology Assessment	Austria	http://hta.lbg.ac.at/en/index.php
KCE	Belgian Health Care Knowledge Centre	Belgium	http://www.kce.fgov.be/index_en.aspx?SGREF=5212
	Le Centre d'expertise des soins de sante	Belgium	https://kce.fgov.be/search/apachesolr_search/?filters=type:biblio%20ss_biblio_secondary_title:"KCE%20Reports"&retain-filters=1
ACFP	Alberta College of Family Physicians	Canada	http://www.acfp.ca/tools-for-practice/
AHW	Alberta Health and Wellness	Canada	http://www.health.alberta.ca/initiatives/AHTDP-reviews.html
BCEOHRN	BC Environmental and Occupational Health Research Network	Canada	http://www.bceohrn.ca/search/greylit/org
CADTH	Canadian Agency for Drugs and Technologies in Health	Canada	http://www.cadth.ca/
CAHSPR	Canadian Association for Health Services & Policy Research	Canada	http://www.cahspr.ca/PublicationsResources/tabid/110/language/en-US/Default.aspx
CP	Canadian Pharmacogenomics Network for Drug Safety	Canada	http://www.cpnds.ubc.ca/index.php?option=com_joomap&Itemid=28.html

UBC	Centre for Blood Research	Canada	http://vp04.cbr.ubc.ca/research_pyenson.htm
CHEPA	Centre for Health Economics and Policy Analysis	Canada	http://www.chepa.org/Research-Products/Publications.aspx
CHSPR	Centre for Health Services & Policy Research, UBC	Canada	http://www.chspr.ubc.ca/pubs/pub-search
CMMT	Centre for Molecular Medicine & Therapeutics	Canada	http://www.cmmt.ubc.ca/
CFRI	Child Family Research Institute	Canada	http://www.cfri.ca/POPi/publications
CMA	Canadian Medical Association	Canada	https://www.cma.ca/En/Pages/SearchPage.aspx?k=tpmt
GC	Government of Canada	Canada	http://recherche-search.gc.ca/rGs/s_r?st=s&s5bm3ts21rch=x&num=10&st1rt=0&langs=eng&cdn=health&q=thiopurine
HC	Health Canada	Canada	http://recherche-search.gc.ca/rGs/s_r?st=s&s5bm3ts21rch=x&num=10&st1rt=0&langs=eng&cdn=health&q=tpmt
HQO	Health Quality Ontario	Canada	http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations
HQO/MAS	Health Quality Ontario, Medical Advisory Secretariat	Canada	http://www.hqontario.ca/en/mas/mas_ohtas_mn.html
HQCA	Health Quality Council of Alberta	Canada	http://www.mcgill.ca/tau/publications/
HLWIKI	HLWIKI International	Canada	http://hlwiki.slais.ubc.ca/index.php?title=Grey_literature
ICES	Institute for Clinical Evaluative Sciences	Canada	http://www.ices.on.ca/
IWH	Institute for Work and Health	Canada	http://www.iwh.on.ca/products/product.php
IHE	Institute of Health Economics	Canada	http://www.ihe.ca/publications/library/
MCHP	Manitoba Centre for Health Policy	Canada	http://umanitoba.ca/medicine/units/mchp/
MUHC	McGill University Health Centre	Canada	http://www.mcgill.ca/tau/publications/
CHEPA	McMaster University - Centre for health Economics and Policy Analysis	Canada	http://www.chepa.org/research-papers/faculty-publications
CCH - MUN	Memorial University of Newfoundland - Community Health and Humanities - Annual Report	Canada	http://www.med.mun.ca/getattachment/73b06990-7f8b-4670-893c-53da20c6cbaf/CHH_AnnualReport_2012_webcolour.a

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MOH	MOH Ontario	Canada	http://www.health.gov.on.ca/
NLCAHR	Newfoundland and Labrador Centre for Applied Health Research	Canada	http://www.nlcahr.mun.ca/CHRSP/CompletedCHRSP.php
OCCI	Ontario Ministry of Health and Long Term Care	Canada	http://www.occp.com/mainPage.htm
OPENMED	Open Medicine	Canada	http://www.openmedicine.ca/search
OHRI	Ottawa Hospital Research Institute	Canada	http://www.ohri.ca/search.asp?searchterm=thiopurine&search.x=0&search.y=0
PATH	Program for Assessment of Technology in Health (Canada)	Canada	http://www.path-hta.ca
PHAC	Public Health Agency of Canada	Canada	http://www.phac-aspc.gc.ca/index-eng.php
HQC	Saskatchewan Health Quality Council	Canada	http://hqc.sk.ca/resources/publications-reports/
MUHC	<u>Technology Assessment Unit of the McGill University Health Centre</u>	Canada	http://www.mcgill.ca/tau/publications/
	The Institut national d'excellence en sante et en service sociaux	Canada	http://www.inesss.qc.ca/index.php?id=49&L=1
	Therapeutics Initiative	Canada	http://www.ti.ubc.ca/TherapeuticsLetter
UBC	<u>Therapeutics Initiative, University of British Columbia</u>	Canada	http://www.ti.ubc.ca/TherapeuticsLetter
THETA	Toronto Health Economics and Technology Assessment Collaborative	Canada	http://theta.utoronto.ca/content.php?pid=411861&sid=3372336
UBC	University of British Columbia	Canada	http://www.ubc.ca/search/?q=thiopurine
UC	University of Calgary	Canada	http://libguides.ucalgary.ca/greylit
UWO	University of Waterloo	Canada	http://subjectguides.uwaterloo.ca/health
NRGL	National Repository of Grey Literature	Czech Republic	http://www.nusl.cz/?lang=en
DACEHTA	Danish Centre for Health Technology Assessment, National Board of Health	Denmark	http://www.sst.dk/English/DACEHTA.aspx
DHMA	Danish Health and Medicines Authority, Sundhedsstyrelsen	Denmark	http://sundhedsstyrelsen.dk/en/publications

INAHTA	(International Network of Agencies for Health Technology Assessment)	EU	http://www.inahta.org/
	Comite d'evaluation de diffusion des Innovations technologiques	France	http://cedit.aphp.fr/cedit-hospital-based-hta-agency/recommendations-reports/
CEDIT	Committee for Evaluation and Diffusion of Innovative Technologies (CEDIT) / Comité d'Evaluation et de Diffusion des Innovations Technologiques	France	http://cedit.aphp.fr/english/index_present.html
HAS	Haute Autorité de santé / French National Authority for Health	France	http://www.has-sante.fr/portail/jcms/c_946986/english-toutes-nos-publications-ligne-principale?portal=c_226237
DIMDI	Deutsches Institut für Medizinische Dokumentation und Information	Germany	http://www.dimdi.de/dynamic/en/hta/db/index.htm
DIMDI	German Institute of Medical Documentation and Information, Federal Ministry of Health	Germany	http://www.dimdi.de/dynamic/en/hta/db/index.htm
	Health Economics - Places to Go-University of Bayreuth	Germany	http://www.medecon.de/hec.htm
	Collège des Economistes de la Santé	International	http://www.ces-asso.org/Publications
	Cost-effectiveness Analysis (CEA) Registry	International	https://research.tufts-nemc.org/cear/default.aspx
	EuroScan Secretariat	International	http://www.euroscan.org.uk/
Google	Google/Google Scholar	International	www.google.ca
INAHTA	INAHTA Secretariat	International	http://www.inahta.org/
LILACS	Latin America and Caribbean Center on Health Sciences Information	International	http://bases.bireme.br/cgi-bin/wxislind.exe/iah/online/?IsisScript=iah/iah.xis&base=LILACS&lang=l
USCN	Life Science Inc.	International	http://www.uscnk.com/directory/Thiopurine-methyltransferase-thiopurine-S-methyltransferase%28TPMT%29-2821.htm
NRLS	National Reporting and Learning Service: National Patient Safety Agency	International	http://www.nrls.npsa.nhs.uk/alerts/
Quest Diagnostics	Quest Diagnostics	International	http://www.questdiagnostics.com/testcenter/testguide.action?dc=TS_TPMT_Activity

OpenGrey	System for Information on Grey Literature in Europe	International	http://www.opengrey.eu/search/request?q=thiopurine
UpToDate	UpToDate	International	http://www.uptodate.com/contents/6-mercaptopurine-6-mp-metabolite-monitoring-and-tpmt-testing-in-the-treatment-of-inflammatory-bowel-disease-with-6-mp-or-azathioprine
WHO	<u>WHO Health Evidence Network</u>	International	http://www.euro.who.int/en/what-we-do/data-and-evidence/health-evidence-network-hen/publications/evidence-reports
WHO	World Health Organization	International	http://www.who.int/genomics/research/treatmentandtechnology/en/
WHO-CHOICE	World Health Organization – Choosing Interventions that are Cost Effective	International	http://www.who.int/choice/en
WHO	World Health Organization Regional Office for Europe	International	http://www.euro.who.int/en/data-and-evidence/evidence-informed-policy-making/publications/by-keyword
WWS	World Wide Science - The Global Science Gateway	International	http://worldwidescience.org/
	Health Information and Quality Authority	Ireland	http://www.hiqa.ie/healthcare/health-technology-assessment/assessments
HSE	<u>Health Service Executive</u>	Ireland	http://www.hse.ie/eng/services/Publications/
	Health Services Executive	Ireland	http://www.lenus.ie/hse/
HSE	Irish Health Repository, Health Services Executive (Lenus)	Ireland	http://www.lenus.ie/hse/
CVZ	College voor zorgverzekeringen (CVZ)	Netherlands	http://www.cvz.nl/publications+in+english
	De Gezondheidsraad (BR), Health Council of the Netherlands	Netherlands	http://www.gezondheidsraad.nl/en
GreyNet	Grey Literature Network Service	Netherlands	http://www.greynet.org/
	<u>Health Council of the Netherlands</u>	Netherlands	http://www.gezondheidsraad.nl/en
	Nasional kunnskapssenter for helsentienesten Norwegian Knowledge Centre for the Health Services	Norway	http://www.kunnskapssenteret.no/publikasjoner?language=english&reportsandnotes=1
	<u>Norwegian Knowledge Centre for the Health</u>	Norway	http://www.kunnskapssenteret.no/Forsiden

	<u>Services</u>		
NZHTA	New Zealand Health Technology Assessment	NZ	http://www.horizonscanning.gov.au/internet/horizon/publishing.nsf/Content/nzhta-2
	Agencia d'Avaluacio de tecnologia I Recerca Mediques de Catalunya	Spain	http://publicaciones.isciii.es/
CAHTA	Catalan Agency for Health Technology Assessment (CAHTA)	Spain	http://www.gencat.cat/salut/depsan/units/aatrm/html/en/dir393/
CMT	Centre for Medical Technology Assessment	Sweden	http://www.cmt.liu.se/pub/jsp/polopoly.jsp?d=6199&l=en
SBU	<u>Swedish Council on Technology Assessment in Health Care</u>	Sweden	http://www.sbu.se/en/
	Swiss Federal Office of Public Health	Switzerland	http://www.snhta.ch/resources/overview.html
	<u>Swiss Network for Health Technology Assessment</u>	Switzerland	http://www.snhta.ch/resources/overview.html?type=
ARIF	Aggressive Research Intelligence Facility	UK	http://www.arif.bham.ac.uk
<u>ATTRACT</u>	<u>National Health Services for Wales</u>	UK	http://www.attract.wales.nhs.uk
Bandolier	Bandolier Knowledge	UK	http://www.medicine.ox.ac.uk/bandolier/knowledge.html
BLDSC	British Library Document Supply Centre	UK	www.bl.uk/reshelp/atyourdesk/docsupply/collection/rct/
CEP	CEP	UK	http://nhscep.useconnect.co.uk/CEPProducts/Catalogue.aspx
CRD	CRD	UK	http://www.crd.york.ac.uk/CRDWeb/
DoH	Dept of Health, UK Government (formerly Research & Development Directorate, NHS Executive South West, Publications)	UK	http://www.dh.gov.uk/PublicationsAndStatistics/Publications/fs/en
EUROSCAN	The European Information Network on New and Changing Health Technologies	UK	http://www.euroscan.bham.ac.uk/technology.htm
HERC	Health Economics Research Centre	UK	http://www.herc.ox.ac.uk/pubs
HERG	Health Economics Research Group	UK	http://www.brunel.ac.uk/about/acad/herg/publications

HERU	Health Economics Research Unit, University of Aberdeen	UK	http://www.abdn.ac.uk/heru/publications/
HK-UK	Health Knowledge UK	UK	http://www.healthknowledge.org.uk/public-health-textbook/research-methods/1a-epidemiology/grey-literature
NCCHTA	<u>NIHR Coordinating Centre for Health Technology Assessment</u>	UK	http://www.hta.ac.uk/
NHS	NHS Centre for Evidence-based Purchasing	UK	http://nhscep.useconnect.co.uk/CEPPProducts/Default.aspx
NHS	National Health Service for Wales	UK	http://www.attract.wales.nhs.uk/
NHS HTA	NHS HTA Programme	UK	http://www.ncchta.org/
NHSC	<u>The National Horizon Scanning Centre</u>	UK	http://www.pcpoh.bham.ac.uk/publichealth/horizon/outputs/technology.shtml
NHSC	NHSC	UK	http://nhsc.hrsa.gov/
NICE	National Institute for Health and Care Excellence	UK	http://www.nice.org.uk/mpc/evidencesummariesnewmedicines/home.jsp
NICE	National Institute for Health and Care Excellence	UK	http://www.nice.org.uk/
NICE	National Institute for Health and Care Excellence	UK	http://www.nice.org.uk/
NIHR	NIHR Evaluation	UK	http://www.nets.nihr.ac.uk/projects?collection=netscc&meta_P_sand=Project
WMCSU	West Midlands Commissioning Support Unit	UK	http://www.birmingham.ac.uk/research/activity/mds/projects/HaPS/PHEB/WMCSU/index.aspx
WMHTAC	<u>West Midlands Health Technology Assessment Collaboration</u>	UK	http://www.wmhtac.bham.ac.uk/
	Centre for Epidemiology & Health Service Research, Brunel University	UK	http://www.brunel.ac.uk/about/acad/health/healthres/researchareas/ehsrg
	Department of Primary Care and Population Sciences	UK	http://www.ucl.ac.uk/pcph/publications/index.htm
	List of International HTA Agencies	UK	http://www.shef.ac.uk/scharr/ir/htaorg.html
	Healthcare Improvement Scotland	UK	http://www.healthcareimprovementscotland.org

AHRQ	Agency for Healthcare Research and Quality	USA	http://www.ahrq.gov/research/findings/ta/
AHRQ	National Guideline Clearinghouse	USA	http://www.guideline.gov/
CePOR	Center for Pharmaceutical Outcomes Research	USA	http://research.unc.edu/services/publications.php
CMS	Centers for Medicare and Medicaid Services	USA	http://www.cms.gov/medicare-coverage-database/indexes/technology-assessments-index.aspx?TAId=85&bc=AAAQAAAAAAAA&
CTAF	California Technology Assessment Forum	USA	http://www.medscape.com/viewpublication/30144
DU	Duke University	USA	http://guides.mclibrary.duke.edu/greyliterature
DVA	Department of Veterans Affairs Research & Development General publications	USA	http://www.research.va.gov/resources/pubs/default.cfm
ECRI	<u>ECRI Institute</u>	USA	http://www.ecri.org/
FDA	US Food & Drug Administration	USA	http://www.fda.gov/opacom/7pubs.html
GT	Georgetown	USA	http://researchguides.dml.georgetown.edu/content.php?pid=352972&sid=2887419
ICER	Institute for Clinical and Economic Review	USA	http://www.icer-review.org/
ICSI	<u>Institute for Clinical Systems Improvement</u>	USA	http://www.icsi.org/guidelines_and_more/technology_assessment_reports/
LDI	Leonard Davis Institute of Health Economics, University of Pennsylvania	USA	http://www.upenn.edu/ldi/publications.html
Mayo clinic	Mayo Clinic	USA	http://www.mayoclinic.org/
MTPPI	Medical Technology and Practice Patterns Institute	USA	http://www.mtppi.org/new/pub.html
NACHRI	National Association of Children's Hospitals and Related Institutions (NACHRI)	USA	http://www.childrenshospitals.net/AM/Template.cfm?Section=Publications2&Template=/TaggedPage/TaggedPageDisplay.cfm&TPLID=204&ContentID=45300
NIH	National Institutes of Health	USA	http://nihpublications.od.nih.gov/search.aspx?welTab=Welcome
NIH	National Institutes of Health	USA	http://www.nih.gov/
NIH	National Institutes of Health	USA	http://www.uniprot.org/uniprot/P51580
NYAM	New York Academy of Medicine	USA	http://www.greylit.org/publishers/list

OMIM	Online Mendelian Inheritance in Man	USA	http://www.omim.org/entry/610460
PharmGKB	The Pharmacogenomics Knowledgebase	USA	https://www.pharmgkb.org/
TEC	<u>Technology Evaluation Center</u>	USA	http://www.bcbs.com/blueresources/tec/vols/
UC	University of Connecticut	USA	http://ideas.repec.org/
UHC	<u>University Health System Consortium</u>	USA	http://www.uhc.edu
US NLM	US NLM	USA	http://www.ncbi.nlm.nih.gov/pubmed
UT	University of Texas	USA	http://www.lib.utexas.edu/chem/info/gray.html
VATAP	VA Technology Assessment Program	USA	http://www.va.gov/vatap/publications.htm
	EPC Topics in Process	USA	http://www.ahrq.gov/clinic/epc/epcprogress.htm
	Evidence-based Practice Centers' evidence reports and technology assessments	USA	http://www.ahrq.gov/clinic/epcquick.htm
	Health Services Research Resources-Leonard Davis Institute of Health Economics	USA	http://www.upenn.edu/ldi/hsr.html
	Blue Cross and Blue Shield Association	USA	http://www.bcbs.com/blueresources/tec/topic.html
	Washington State Health Care Authority	USA	http://www.hca.wa.gov/hta/Pages/Forms/HTA_Findings.aspx
ARUP	Laboratory Test Directory		http://ltd.aruplab.com/Tests/Pub/0092066
CC	Cochrane Collaboration		http://www.cochrane.org/search/site/thiopurine
DocuTicker	DocuTicker		http://www.docuticker.com/
Ghor	Grey Horizon		http://grey-horizon.blogspot.nl/
	clinical chem		http://www.clinchem.org/content/47/5/956.full

Appendix C – Extracted Data

Variable	Description
Author1_LastName	Family name of primary author
Author1_FirstName	
Author2_LastName	
Author2_FirstName	
AuthorsAdditional	
Title	
PublicationYear	Year the study was published
Journal	Journal name
Volume	Volume of journal
Issue	Issue (if applicable)
PageStart	First page of the article in publication
PageEnd	Last page of the article in publication
Organization	Organization conducting the study
StudyFoundWhere	How the study was found (grey literature search, systematic review)
Category	Type of comparator used in this study (genotype-phenotype, ADE, or different laboratory method)
3x3_Data	Indicate whether data is available to populate a 2x2 or 3x3 table.
2nd_Reviewer3x3	Indicate if second reviewer is requested to confirm 3x3 table
2ndReview_Quadas	Second QUADAS reviewer required for this study?
2ndReview_Quadas_Comment	Comments for second reviewer to indicate reason for second review
Include_BasisQuality	Should this study be included based on quality assessment?
Include_BasisQualityComment	Comment on decision to include or exclude study.
Notes	Additional notes regarding quality assessment.
StudyDesign	*Indicate how the design of this study is described
StudyDesignOther	*Describe any additional aspects of the study design
PrimaryObjective	*Primary objective
SecondaryObjective	*Secondary objective

InclusionCriteria	*Describe inclusion criteria
ExclusionCriteria	*Describe exclusion criteria, if applicable
TargetGender	*Gender targeted, if applicable
TargetRaceGroup	
PhenotypeTestUnitMeasure	*List the unit of measure for the phenotype test
PurposeTest1	Describe comparator e.g. low vs high TPMT
ReportedSens1	Reported sensitivity, if reported
ReportedSens_UncertMeas1	
ReportedSens_UncertLowBound1	
ReportedSens_UncertUppBound1	
ReportedSpec1	Reported specificity, if reported
ReportedSpec_UncertMeas1	
ReportedSpec_UncertLowBound1	
ReportedSpec_UncertUppBound1	
PPV1	Positive predictive value
NPV1	Negative predictive value
Concordance1	
PurposeTest2	Describe comparator e.g. low vs high TPMT
NumIdentified	*Number of potential study participants identified (if specified)
NumIncluded	Total number of subjects included/enrolled in the study
SampleAgeGroup	*Indicate the age group of the sample population
SampleAverageAge	Average age of the study sample
SampleMale	% male
SampleRaceGroups	*Indicate the ethnicity of the sample population
SampleEthnicGroups	
NumWithTargetDisease	*Number of participants with the target disease
PhenotypeContinuousData	Yes/No (present/absent in paper)
ContingencyTableProvided	Yes/No (present/absent in paper)

d1_RecruitLocation	Patient selection: Describe where the study took place. e.g. country, clinic, etc. Clearly state if "not specified".
d1_SampleMethod	*Patient selection: How did the researchers recruit subjects? Clearly state if "not specified".
d1_TimePeriod	Patient selection: Over what time period did the study take place (e.g. over 3 months, over 1 year). Identify dates where possible. Clearly state if "not specified".
d1_PtSelectionAddlInfo	Patient selection: Describe any additional relevant methods of patient selection.
d1q1_RandomSample	*Was a consecutive or random sample of subjects enrolled during overall recruitment?
d1q1_Comment	
d1q2_CaseCtrlAvoided	*Was a case-control design avoided?
d1q2_Comment	
d1q3_InappropExclAvoided	*Did the study avoid inappropriate exclusions during overall recruitment?
d1q3_Comment	
d1q4_RandomExcl	Did the exclusions (if any) appear random?
d1q4_Comment	
d1_BiasRisk	*Could the selection of patients have introduced bias?
d1_BiasComment	
d1_Disease	*Included subjects: Select the disease group included in the study. Clearly state if "not specified".
d1_DiseaseOther	
d1_Age	*Included subjects: Select the age group which best describes the subjects entered in the study. Clearly state if "not specified".
d1_Group	*Included subjects: Describe the type of subjects included (e.g. cardiac patients, general public). Clearly state if "not specified".
d1_EthnicityOrRace	*Included subjects: Identify if a particular ethnicity or race was targeted. Clearly state if "not specified".
d1_EthnicityOrRaceOther	

d1_Relation	*Included subjects: Are subjects related to each other? Clearly state if "not specified".
d1_SubjectAdditionalInfo	Included subjects: Describe any additional relevant information on included patients (prior testing, presentation).
d1_ApplicabilityConcern	*Is there concern that the included patients do not match the review question?
d1_ApplicabilityComment	
d2_SampleSource	*Describe index test: From what was the sample taken from? e.g. red blood cells, leucocytes, etc.
d2_AmplificationMethod	*Describe index test: describe the amplification method.
d2_GenotypeMethod	*Describe index test: describe the specific genotype method used (e.g. Taq, HPLC, etc)
d2_GenotypeMethodOther	Index test: if genotype method "other", list genotype method used
d2_PolymorphismsTested	*Describe index test: Which polymorphisms were tested for? Select all that apply.
d2_PolymorphismsOther	Index test: if polymorphisms "other", list polymorphisms tested
d2_IndexTestAdditionalInfo	Describe the index test: additional information on how it was conducted and interpreted.
d2q1_PolymorphSpecified	Were the polymorphisms tested specified a priori?
d2q1_Comment	
d2q2_CompleteScan	Was a complete scan of the TPMT gene conducted (versus specific polymorphisms tested)?
d2q2_Comment	
d2_BiasRisk	*Could the conduct or interpretation of the index test have introduced bias?
d2_BiasComment	
d2_ApplicabilityConcern	*Is there concern that the index test, its conduct, or interpretation differ from the review question?
d2_ApplicabilityComment	

Domain 3	
d3_SampleSource	*Describe reference standard: Indicate what kind of sample was used for the test (e.g. leucocytes, EDTA blood, etc)
d3_PhenotypeMethod	*Describe reference standard: Select the method of phenotyping used. Clearly indicate if not specified
d3_PhenotypeMethodOther	*Included subjects: if phenotype method "other", list phenotype method used.
d3_SubstrateUsed	*Describe reference standard: Indicate which substrate(s) were used to identify phenotype. Clearly indicate if not specified.
d3_SubstrateUsedOther	Included subjects: if substrate used "other", list substrate used.
d3_RefAddtnlInfo	Describe reference standard: additional information on how it was conducted and interpreted:
d3_Cutpoints	*Indicate all cut-points used to identify levels of TPMT activity. Clearly indicate if not specified.
d3_CutpointsOther	If cutpoints "other", describe cutpoints used.
d3q1_RefCorrectlyClassifies	*Is the reference standard likely to correctly classify the target condition?
d3q1_Comment	
d3q2_ThresholdsDefined	Were thresholds defined a priori?
d3q2_Comment	
d3q3_AllClassified	Were all phenotype results given a classification? (e.g. normal/low/deficient).
d3q3_Comment	
d3_BiasRisk	*Could the reference standard, its conduct, or its interpretation have introduced bias?
d3_BiasComment	
d3_ApplicabilityConcern	*Is there concern that the target condition as defined by the reference standard does not match the review question?
d3_ApplicabilityComment	
d4_PatientsExcluded	Describe any patients who did not receive the index test(s) and/or reference standard or who were excluded from the 2x2 table (refer to flow diagram):

d4_TimeIntervalBtwn	Describe the time interval and any interventions between index test(s) and reference standard?
d4q1_AllReceivedReference	*Did all patients receive a reference standard?
d4q1_Comment	
d4q2_AllReceivedSameReference	*Did patients receive the same reference standard?
d4q2_Comment	
d4q3_AllIncludedInAnalysis	*Were all patients included in the analysis?
d4q3_Comment	
d4q4_InapExcAvoided	*Were inappropriate exclusions avoided?
d4q4_Comment	
d4q5_AnalyzeTarget	Did we analyze the same population that was recruited?
d4q5_Comment	
d4_BiasRisk	*RISK: high/low/unclear - could the patient flow have introduced bias?
d4_BiasComment	
d5_ClearIdentificationRace	* Did the study clearly identify the racial or ethnic population being studied?
d5_PolymorphismsIdentified	*If specific polymorphisms were tested, were they identified a priori?
d5_ClearClassificationResults	* Was the classification of genetic test results (homozygous/heterozygous/wild type or genetic score) described clearly?
d5_SelectiveGenotyping	*Did the study avoid selective genotyping after establishing phenotype (or vice versa)?
d5_AllPolymorphismsTested	* Were all polymorphisms of interest tested?
d5_BiasRisk	*RISK: high/low/unclear - could genomic-specific process have introduced bias?
d5_BiasComment	
DataDescription	title or description of group belonging to the data in these cells/this table
LO	number of patients with phenotype low TPMT
INT	number of patients with phenotype intermediate TPMT
HI	number of patients with phenotype normal TPMT

Ho	number of patients with genotype homozygous deficient TPMT
He	number of patients with genotype heterozygous deficient TPMT
WT	number of patients with genotype wild type TPMT
LO-Ho	low phenotype and homozygous deficient
LO-He	low phenotype and heterozygous
LO-WT	low phenotype and wildtype
INT-Ho	intermediate phenotype and homozygous deficient
INT-He	intermediate phenotype and heterozygous
INT-WT	intermediate phenotype and wildtype
HI-Ho	high phenotype and homozygous deficient
HI-He	high phenotype and heterozygous
HI-WT	high phenotype and wildtype
total	grand total tested.
AuthorLastName	Last name of author
MethodCat	What category of methods were being compared?
StudyDescription	General description of the study
Ind1_Method	
Ind1_Substrate	
Ind1_sample	
Ind1_UnitAssay	
Ind1_AddDescription	
Ref1_Method	
Ref1_Substrate	
Ref1_sample	
Ind2_Method	Additional methods compared, if applicable
Ind3_Method	
Disease	Disease
Age	

Race	
HumanSubjects	
AllMethodsCategorized	Were all methods used given a clear classification (hi/int/lo, ho/he/wt)?
NumPatients	
Cutoff_Hi-Int	Cut-off value between High-Intermediate phenotype
Cutoff_Int-Lo	Cut-off value between Intermediate-Low phenotype
Cutoff_Hi-VeryHi	Cut-off value between Hi-VeryHigh phenotype, where applicable
3x3Data	Is there sufficient comparison data to create 3x3/2x2 tables?
ScreenDecision1	Initial screening for presence of comparison and sufficient 3x3 data
ScreenDecision2	If required, screening by second reviewer for presence of comparison and sufficient 3x3 data
TableNum	
DataDescription	
Lo/Ho (V)	Total low activity (or homozygous)
Int/He (V)	Total intermediate activity (or heterozygous)
Hi/WT (V)	Total high activity (or wild-type)
Lo/Ho (H)	Total low activity (or homozygous)
Int/He (H)	Total Intermediate activity (or heterozygous)
Hi/WT (H)	Total High activity (or wild-type)
Lo/Ho-Lo/Ho2	Low activity (or homozygous) low activity (or homozygous)
Lo/Ho-Int/He2	Low activity (or homozygous) intermediate activity (or heterozygous)
Lo/Ho-Hi/WT2	Low activity (or homozygous) high activity (or wild-type)
Int/He-Lo/Ho2	Intermediate activity/heterozygous low activity/homozygous
Int/He-Int/He2	Intermediate activity/heterozygous intermediate activity/heterozygous
Int/He-Hi/WT2	Intermediate activity/heterozygous intermediate activity/wild-type
Hi/WT-Lo/Ho2	High activity/wild-type low activity/homozygous
Hi/WT-Int/He2	High activity/wild-type intermediate activity/heterozygous
Hi/WT-Hi/WT2	High activity/wild-type high activity/wild-type
Total	

Appendix D – Modified QUADAS-2

Domain 1 – Patient Selection

Patient selection information:

- Describe where the study took place. E.g. country, clinic, etc. Clearly state if "not specified". (var: d1_RecruitLocation)

- How did the researchers recruit subjects? Clearly state if "not specified". (var: d1_SampleMethod)

- Over what time period did the study take place (e.g. over 3 months, over 1 year). Identify dates where possible. Clearly state if "not specified". (var: d1_TimePeriod)


- Describe any additional relevant methods of patient selection. (var: d1_PtSelectionAddlInfo)

A. Risk of Bias *TO BE COMPLETED BY REVIEWERS*

Question	Response	Variable Name
❖ *Was a consecutive or random sample of subjects enrolled during overall recruitment?	<input type="checkbox"/> Yes	d1q1_RandomSample
	<input type="checkbox"/> No	
	<input type="checkbox"/> Unclear	
	(Free text)	d1q1_Comment
❖ *Was a case-control design avoided?	<input type="checkbox"/> Yes	d1q2_CaseCtrlAvoided
	<input type="checkbox"/> No	
	<input type="checkbox"/> Unclear	
	(Free text)	d1q2_Comment
❖ *Did the study avoid inappropriate exclusions during overall recruitment?	<input type="checkbox"/> Yes	d1q3_InappropExclAvoided
	<input type="checkbox"/> No	
	<input type="checkbox"/> Unclear	
	(Free text)	d1q3_Comment
❖ Did the exclusions (if any) appear random?	<input type="checkbox"/> Yes	d1q4_RandomExcl
	<input type="checkbox"/> No	

	<input type="checkbox"/> Unclear	
	(Free text)	d1q4_Comment
*Could the selection of patients have introduced bias?	<input type="checkbox"/> RISK LOW	d1_BiasRisk
	<input type="checkbox"/> RISK HIGH	
	<input type="checkbox"/> RISK UNCLEAR	
	(Free text)	d1_BiasComment

Information on subjects included in study:

 ***Select the disease group included in the study. Clearly state if "not specified". (var: d1_Disease)**


- Dermatological conditions
- Rheumatoid Arthritis (RA)
- Acute lymphoblastic leukemia (ALL)
- Inflammatory bowel disease (IBD)
- Organ transplant
- Otherwise healthy
- Other
- Not specified

 ***If disease "other", list disease groups included. (var: d1_DiseaseOther)**

 **Select the age group which best describes the subjects entered in the study. Clearly state if "not specified". (var: d1_Age)**


- Adult
- Pediatric
- Mix of adult and pediatric
- Not specified

 ***Describe the type of subjects included (e.g. cardiac patients, general public). Clearly state if "not specified". (var: d1_Group)**

 ***Identify if a particular ethnicity or race was targeted. Clearly state if "not specified". (var: d1_EthnicityOrRace)**

- Native American
- European
- African
- German
- Chinese
- Ashkenazi Jewish
- North American
- Spanish

- Norwegian
- Middle Eastern
- Caucasian
- Black
- Asian
- Other
- Not specified

 ***If ethnicity or race "other", list ethnic or racial groups included (var: d1_EthnicityOrRaceOther)**

 ***Are subjects related to each other? Clearly state if "not specified". (var: d1_Relation)**

- Related
- Unrelated
- Not specified


 ***Describe any additional relevant information on included patients (prior testing, presentation). (var: d1_SubjectAdditionalInfo)**

B. Concerns regarding applicability *TO BE COMPLETED BY REVIEWERS*


Question	Response	Variable Name
*Is there concern that the included patients do not match the review question?	<input type="checkbox"/> CONCERN LOW	d1_ApplicabilityConcern
	<input type="checkbox"/> CONCERN HIGH	
	<input type="checkbox"/> CONCERN	
	UNCLEAR	
	(Free text)	d1_ApplicabilityComment

Domain 2 – Index Test(s)

Describe index test:


-  *From what was the sample taken from? e.g. red blood cells, leucocytes, etc. (var: d2_SampleSource)

-  *Describe the amplification method. (var: d2_AmplificationMethod)

-  *Describe the specific genotype method used (e.g. Taq, HPLC, etc). (var: d2_GenotypeMethod)

- Taq
- Restriction mapping/analysis/digest
- Polymerase chain reaction (PCR)
- Fluorescence
- Other
- Not specified

-  *If genotype method "other", list genotype method used. (var: d2_GenotypeMethodOther)

-  *Which polymorphisms were tested for? Select all that apply. (var: d2_PolymorphismsTested)

- TPMT*1
- TPMT*2
- TPMT*2a
- TPMT*2b
- TPMT*3
- TPMT*3a
- TPMT*3b
- TPMT*3c
- TPMT*3d
- TPMT*6
- TPMT*7
- Other
- Not specified

 ***If polymorphisms "other", list polymorphisms tested. (var: d2_PolymorphismsOther)**

 ***Additional information on how it was conducted and interpreted. (var: d2_IndexTestAdditnlInfo)**

A. Risk of Bias *TO BE COMPLETED BY REVIEWERS*

Question	Response	Variable Name
❖ Were the polymorphisms tested specified a priori?	<input type="checkbox"/> Yes	d2q1_PolymorphSpecified
	<input type="checkbox"/> No	
	<input type="checkbox"/> Unclear	
		d2q1_Comment
❖ Was a complete scan of the TPMT gene conducted (versus specific polymorphisms tested)?	<input type="checkbox"/> Yes	d2q2_CompleteScan
	<input type="checkbox"/> No	
	<input type="checkbox"/> Unclear	
	(Free text)	d2q2_Comment
*Could the conduct or interpretation of the index test have introduced bias?	<input type="checkbox"/> RISK LOW	d2_BiasRisk
	<input type="checkbox"/> RISK HIGH	
	<input type="checkbox"/> RISK UNCLEAR	
	(Free text)	

B. Concerns regarding applicability *TO BE COMPLETED BY REVIEWERS*

Question	Response	Variable Name
*Is there concern that the index test, its conduct, or interpretation differ from the review question?	<input type="checkbox"/> CONCERN LOW	d2_ApplicabilityConcern
	<input type="checkbox"/> CONCERN HIGH	
	<input type="checkbox"/> CONCERN UNCLEAR	
	(Free text)	

Domain 3 – Reference Standard

Describe reference standard:

- *Indicate what kind of sample was used for the test (e.g. leucocytes, EDTA blood, etc). (var: d3_SampleSource)

- *Select the method of phenotyping used. Clearly indicate if not specified. (var: d3_PhenotypeMethod)

- High pressure liquid chromatography (HPLC)
- Mass spectrometry
- Radiochemical method
- Other
- Not specified

- *If phenotype method "other", list phenotype method used. (var: d3_PhenotypeMethodOther)

- *Indicate which substrate(s) were used to identify phenotype. Clearly indicate if not specified. (var: d3_SubstrateUsed)

- 6-thioguanine (6TG)
- 6-mercaptopurine (6MP)
- Other
- Not specified

- *If substrate used "other", list substrate used. (var: d3_SubstrateUsedOther)


- *Additional information on how it was conducted and interpreted. (var: d3_RefAddtnInfo)

- *Indicate all cut-points used to identify levels of TPMT activity. Clearly indicate if not specified. (var: d3_Cutpoints)

- Weinshilboum (HI >10)
- Weinshilboum (HI >9.5)
- > 50 (high)
- > 22 (high), >51 (very high)
- Researchers calculated own cut-point

Other

Cut-point was not specified

 *If cut-points "other", describe cut-points used. (var: d3_CutpointsOther)


A. Risk of Bias *TO BE COMPLETED BY REVIEWERS*

Question	Response	Variable Name
❖ Is the reference standard likely to correctly classify the target condition?	<input type="checkbox"/> Yes	d3q1_RefCorrectlyClassifies
	<input type="checkbox"/> No	
	<input type="checkbox"/> Unclear	d3q1_Comment
	(Free text)	
❖ Were thresholds defined a priori?	<input type="checkbox"/> Yes	d3q2_ThresholdsDefined
	<input type="checkbox"/> No	
	<input type="checkbox"/> Unclear	d3q2_Comment
	(Free text)	
❖ Were all phenotype results given a classification? (e.g. normal/low/deficient).	<input type="checkbox"/> Yes	d3q3_AllClassified
	<input type="checkbox"/> No	
	<input type="checkbox"/> Unclear	d3q3_Comment
	(Free text)	
*Could the reference standard, its conduct, or its interpretation have introduced bias?	<input type="checkbox"/> RISK LOW	d3_BiasRisk
	<input type="checkbox"/> RISK HIGH	
	<input type="checkbox"/> RISK UNCLEAR	d3_BiasComment
	(Free text)	

B. Concerns regarding applicability *TO BE COMPLETED BY REVIEWERS*

Question	Response	Variable Name
*Is there concern that the target condition as defined by the reference standard does not match the review question?	<input type="checkbox"/> CONCERN LOW	d3_ApplicabilityConcern
	<input type="checkbox"/> CONCERN HIGH	
	<input type="checkbox"/> CONCERN UNCLEAR	d3_ApplicabilityComment
	(Free text)	

Domain 4 – Flow and Timing

 ***Describe any patients who did not receive the index test(s) and/or reference standard or who were excluded from the 2x2 table (refer to flow diagram). (var: d4_PatientsExcluded)**

 ***Describe the time interval and any interventions between index test(s) and reference standard? (var: d4_TimeIntervalBtwn)**

A. Risk of Bias *TO BE COMPLETED BY REVIEWERS*

Question	Response	Variable Name
❖ Did all patients receive a reference standard?	<input type="checkbox"/> Yes	d4q1_AllReceivedReference
	<input type="checkbox"/> No	
	<input type="checkbox"/> Unclear	
	(Free text)	d4q1_Comment
❖ Did patients receive the same reference standard?	<input type="checkbox"/> Yes	d4q2_AllReceivedSameReference
	<input type="checkbox"/> No	
	<input type="checkbox"/> Unclear	
	(Free text)	d4q2_Comment
❖ Were all patients included in the analysis?	<input type="checkbox"/> Yes	d4q3_AllIncludedInAnalysis
	<input type="checkbox"/> No	
	<input type="checkbox"/> Unclear	
	(Free text)	d4q3_Comment
❖ Were inappropriate exclusions avoided?	<input type="checkbox"/> Yes	D4q4_InapExcAvoided
	<input type="checkbox"/> No	
	<input type="checkbox"/> Unclear	
	(Free text)	D4q4_Comment
❖ Did we analyze the same population that was recruited?	<input type="checkbox"/> Yes	d4q5_AnalyzeTarget
	<input type="checkbox"/> No	
	<input type="checkbox"/> Unclear	
	(Free text)	d4q5_Comment
*RISK: high/low/unclear - could the patient flow have introduced bias?	<input type="checkbox"/> RISK LOW	d4_BiasRisk
	<input type="checkbox"/> RISK HIGH	
	<input type="checkbox"/> RISK UNCLEAR	
	(Free text)	d4_BiasComment

Domain 5 – Genomics aspects

A. Risk of Bias *TO BE COMPLETED BY REVIEWERS*

Question	Response	Variable Name
❖ Did the study clearly identify the racial or ethnic population being studied?	<input type="checkbox"/> Yes	d5_ClearIdentification
	<input type="checkbox"/> No	Race
	<input type="checkbox"/> Unclear	
❖ If specific polymorphisms were tested, were they identified a priori?	<input type="checkbox"/> Yes	d5_PolymorphismsIdentified
	<input type="checkbox"/> No	
	<input type="checkbox"/> Unclear	
❖ Was the classification of genetic test results (homozygous/heterozygous/wild type or genetic score) described clearly?	<input type="checkbox"/> Yes	d5_ClearClassification
	<input type="checkbox"/> No	Results
	<input type="checkbox"/> Unclear	
❖ Did the study avoid selectively genotyping after establishing phenotype (or vice versa)?	<input type="checkbox"/> Yes	d5_SelectiveGenotyping
	<input type="checkbox"/> No	
	<input type="checkbox"/> Unclear	
❖ Were all polymorphisms of interest tested?	<input type="checkbox"/> Yes	d5_AllPolymorphismsTested
	<input type="checkbox"/> No	
	<input type="checkbox"/> Unclear	
*RISK: high/low/unclear - could genomic-specific process have introduced bias?	<input type="checkbox"/> RISK LOW	d5_BiasRisk
	<input type="checkbox"/> RISK HIGH	
	<input type="checkbox"/> RISK UNCLEAR	
	(Free text)	d5_BiasComment

Summary

TO BE COMPLETED BY REVIEWERS

Legend: L = low, H = high, U = unclear

Risk	Concern for Applicability	Decision	Rationale
LLLL	LLLL	Include	
HHHH	HHHH	Exclude	
UUUU	UUUU	Exclude	
#L = 2,3,4	#L = 2,3,4	Include	
#H = 2,3,4	#H = 2,3,4	Exclude	
#U = 2+	#U = 2+	Exclude	Worse to make judgment on unreported

Appendix E – Decision Rules for Quality Appraisal

Purpose

To ensure consistency in judgment between reviewers throughout the quality assessment process.

Definitions

Index test – the test of interest, newer test, or the test being investigated

Reference test – the test being compared to, which exists as the current status quo or the gold standard

Case-control study: a study comparing two groups - persons with the outcome and persons without the outcome - to retrospectively examine the relationship with a particular exposure. (Gordis 2009 Epidemiology 4th ed.). In the context of this review, the outcome of interest is a particular genotype classification or a particular phenotype classification (e.g. a group of TPMT deficient people, or a group of people with a particular TPMT polymorphism).

Domain 1 – Patient Selection

D1 Questions

d1q1 Was a consecutive or random sample of patients enrolled during overall recruitment?

- “yes”
 - Consecutive, sequential, or random sampling specified for overall study as well as for selection of individuals for each diagnostic test
- “no”
 - Specially selected potentially high-risk individuals
 - Sampling was intentionally designed to get participants with specific TPMT activity levels (x high, x low, etc.)
 - Sampling was in any way that may have increased risk of bias
- “unclear”
 - Sampling method not stated or unclear

d1q2 Was a case-control design avoided?

- *Case control: refer also to definitions above – case control refers to the recruitment of individuals with specific TPMT activity, not individuals with different disease status*
- “yes”
 - Sampling method for each diagnostic test or overall study clearly not selective for a particular genotype or phenotype
- “no”
 - Sampling method for each diagnostic test or overall study reflective of being selective for a particular genotype or phenotype
- “unclear”
 - Sampling method for each diagnostic test or overall study unclear or not specified as to whether it was selective or not for a particular genotype or phenotype

d1q3 Did the study avoid inappropriate exclusions during overall recruitment?

- Consider: “inappropriate” – did their exclusion introduce bias? Were patients with specific genotype or phenotype excluded?
- Consider: Were any exclusions random (versus purposeful)?
- “yes” (if randomly excluded)
- “no” (if selectively excluded)
- “unclear”

D1q4 Did the exclusions (if any) appear random?

d1 Risk of bias

- “Low risk”
 - If all questions in this section answered “yes”
- “High risk”
 - If all questions in this section answered “no”
- “unclear”
 - If any questions in this section answered “unclear”
- If there is a mix of “yes”, “no”, “unclear” → make judgment based on magnitude of risk, and then reach consensus

d1 Concern for applicability – Are there concerns that the included patients and setting do not match the review question?

- “low concern”
 - Included patients and setting clearly match the review question
- “high concern”
 - Included patients and setting clearly *do not* match the review question
- “unclear”
 - Unclear whether patients and setting match the review question

Domain 2 – Index Test(s)

D2q1 Were the polymorphisms tested specified a priori?

- “Yes”
- “No”
- “Unclear”

D2q2 Was a complete scan of the TPMT gene conducted (versus specific polymorphisms tested)?

- ❖ **Consider: complete scan refers to TPMT gene, not the entire/whole genome**
- “Yes”
 - All ten exons investigated
 - 21 known polymorphisms in 2004 [ref Schaeffeler]– TPMT*1, 2, 3A, 3B, 3C, 3D, 4-18
- “No”
 - Less than the full ten exons investigated
 - 21 known polymorphisms in 2004 [ref Schaeffeler] – TPMT*1, 2, 3A, 3B, 3C, 3D, 4-18
- “Unclear”

d2 Risk of bias

- “Low risk”
 - If all questions in this section answered “yes”
 - If previously specified polymorphisms included TPMT*2 and TPMT*3 (which account for >90% polymorphisms)
- “High risk”
 - If all questions in this section answered “no”
- “unclear”
 - If any questions in this section answered “unclear”
- If there is a mix of “yes”, “no”, “unclear” → make judgment based on magnitude of risk, and then reach consensus

d2 Concern for applicability – Are there concerns that the index test, its conduct, or interpretation differ from the review question?

- “low concern”
 - Index test, conduct, and interpretation clearly match the review question
- “high concern”
 - Index test, conduct, and interpretation clearly *do not* match the review question

- “unclear”
 - Unclear whether index test, conduct, and interpretation match the review question
 - If conduct of test unclear

Domain 3 – Reference Standard

d3q1 Is the reference standard (phenotype) likely to correctly classify the condition?

- Consider: did the study classify phenotype based on established classification methods? (versus determining own classification cutoffs)
- “yes”
 - Phenotyping is likely to correctly classify the condition as deficient, intermediate, or high TPMT activity
 - Used conventional, previously validated classification cutoffs
 - Provide a reference for the cutoff chosen (implying they used some previously determined cutoff)
- “no”
 - Phenotyping is unlikely to correctly classify the condition as deficient, intermediate, or high TPMT activity
 - Used new or sample-determined classification cutoffs
 - Sample-determined (i.e. ROC analysis) cutoffs not reason alone for allocation of “high bias” – must have multiple “no/unclear” responses.
- “unclear”
 - Unclear whether phenotyping will correctly classify the target condition as deficient, intermediate, or high TPMT activity

d3q2 Were thresholds defined a priori?

- Consider: were the thresholds explained prior to testing? Were thresholds based on previously validated classification cutoffs?
- “yes”
 - List of cut-off points that will categorize the levels of TPMT activity were pre-specified
 - Any intermediate or high-normal definitions of TPMT activity were pre-specified
- “no”
 - No statement of cut-off points
 - Thresholds/categories for low/intermediate/high TPMT activity not specified a priori
 - Thresholds defined after testing (i.e. ROC analysis of sample results)
- “unclear”
 - Unclear what the cut-off points were, and how many, for phenotype classification
 - Unclear whether thresholds were defined before testing

d3q3 Were all phenotype results given a classification? (e.g. normal/low/deficient).

- “yes”
 - Reference results were classified as normal/low/deficient or some variation
- “no”
 - Reference results did not receive a classification, and only received a numeric (continuous) value for their TPMT activity
- “unclear”
 - If not specified how reference results were presented
 - If reference results were not presented in the results

d3 Risk of bias

- “Low risk”
 - If all questions in this section answered “yes”
- “High risk”
 - If all questions in this section answered “no”
- “unclear”

- If any questions in this section answered “unclear”
- If there is a mix of “yes”, “no”, “unclear” → make judgment based on magnitude of risk, and then reach consensus

d3 Concern for applicability – Are there concerns that the target condition as defined by the reference standard does not match the question?

- “low concern”
 - Target condition as defined by the phenotype test clearly matches the review question
- “high concern”
 - Target condition as defined by the phenotype test clearly *does not* match the review question
- “unclear”
 - Unclear whether target condition as defined by the phenotype test match the review question

Domain 4 – Flow and Timing

d4q1 Did all patients receive a reference standard?

- “yes”
- “no”
- “unclear”

d4q2 Did patients receive the same reference standard?

- “yes”
- “no”
- “unclear”

d4q3 Were all patients included in the analysis? (were all patients who received BOTH TESTS included in the analysis – the exclusion of some patients from receiving both tests is addressed in d4q1 and d4q2)

- “yes”
 - Or, any exclusions were random
- “no”
 - Or, exclusions were non-random
- “unclear”

D4q4 Were inappropriate exclusions avoided?

Consider: if patients or results were excluded from the analysis, did their exclusion cause bias in the results?

- “yes”
 - Exclusions were random, and avoided selection of a specific outcome
- “no”
 - Exclusions were non-random, selective for a specific outcome
- “unclear”

D4q5 Did we analyze the same population that was recruited? Does it affect accuracy, or prevalence of condition?

- “Yes”
 - Or, any exclusions were random
- “No”
 - Or, exclusions were non-random
- “Unclear”

d4 Risk of bias

- “Low risk”

- If all questions in this section answered “yes”
- “High risk”
 - If all questions in this section answered “no”
- “unclear”
 - If any questions in this section answered “unclear”
- If there is a mix of “yes”, “no”, “unclear” → make judgment and comment based on magnitude of risk, and then reach consensus

Domain 5 – Genomics aspects

D5 Risk of bias

- **Not identifying race or ethnic population not basis for high risk of bias as sole factor – must be accompanied by other risks**
- **Not testing for all polymorphisms not basis for high risk of bias as sole factor– must be accompanied by other risks, or must not have tested for TPMT*2 and TPMT*3**

Summary

Legend: L = low, H = high, U = unclear

Risk	Concern for Applicability	Decision	Rationale
LLLL	LLLL	include	
HHHH	HHHH	exclude	
UUUU	UUUU	Exclude	
#L = 2,3,4	#L = 2,3,4	include	
#H = 2,3,4	#H = 2,3,4	exclude	
#U = 2+	#U = 2+	exclude	worse to make judgment on unreported
Mixed U/H	Mixed U/H	??	??