Methotrexate Audit
Collation of all Group Practice Outcomes

The Medicines Optimisation Team (MOT) undertook the Methotrexate audit between November 2020 and January 2021 in order to ascertain and assess the quality of documented safety information on patient medical records in GP practices who are prescribers of Methotrexate.

Introduction of work plan

The National Patient Safety Association (NPSA) published a safety document in July 2004, 'Towards the safer use of oral methotrexate'. This document detailed that oral methotrexate has been associated with a high rate of adverse incidents and even deaths in the NHS and throughout the world due to inappropriate prescribing, dispensing errors, administration errors and failures in appropriate monitoring. There was no suggestion that the drug is unsafe and stated that the efficacy of the drug is not in question and is safe if used in the correct way. According to The National Patient Safety Association (NPSA) it is prescribing and monitoring errors that mostly lead to incidents.

"The most common reason for an incident was an overdose of the drug due to the fact that a weekly dose had been prescribed as a daily dose and a failure or delay in the monitoring of regular blood tests".
(NPSA, 2004).

A part of MOT's role is the responsibility of implementing and monitoring patient safety audits in our GP practices, following MHRA guidance. The results from this audit have allowed MOT to acquire further understanding of the different conditions for which Methotrexate is indicated, the monitoring requirements, variations in dosing and an overall increase in clinical knowledge on this subject.

Patient safety audits are crucial in helping to avoid any adverse medication incidents involving patients as well as highlighting any trends that may lead to a change in current procedure.

Quality improvement

As well as a gain in personal clinical knowledge, on completion of the audit MOT hope to demonstrate an increased awareness of safe Methotrexate prescribing by highlighting and improving the safety information available to GP's, practice staff and patients alike, with the potential of enhancing current systems and processes. Currently there are no local shared-

care policies between primary and secondary care in Isle of Man, we will be looking at local as well as national guidelines during research.

Implementation methods

- Produce an audit template to incorporate GP and hospital agreement for work to be carried out
- Build an EMIS search and compile the audit in order to determine the number of patients prescribed methotrexate, treatment indication, safety warnings and monitoring in place (or not) as well as the quality of directions
- Identify co-prescribing of folic acid and significant interactions such as co-prescribing of co-trimoxazole and trimethoprim
- Ascertain current practice repeat prescribing policies/processes to ensure patient safety as advised by MHRA safety recommendations. Is subcutaneous methotrexate (hospital only) on patients' medical records on the GP EMIS system
- Produce a reflective diary that will detail the planning and reading using the resources listed below, findings of the compiled audit and any scope for quality improvement

Summary of Audit Findings

Patient medical records
- are not always being maintained following changes to prescribing
- are not always being updated when patients stop Methotrexate

Folic Acid
- Incorrect and/or unclear directions as to how the patient is to take Methotrexate, Folic Acid or both, ie, Folic Acid directions state day of week & 'Not to be taken on same day as methotrexate' is often missing
- Unclear as to who is to issue Folic Acid, ie, not in hospital section but issued by GP
- PMR is missing Folic Acid information and/or Hospital letters

Methotrexate
- What is being prescribed does not always mirror what is in the PMR, ie, prescribed 10mg tablets but PMR 2.5mg, or current dose 20mg & S/C, but PMR shows 15mg oral
- records did not provided clear weekly directions stating the day of week Methotrexate was to be taken

Blood Testing
- Some repeat blood tests are out of range

Annual Reviews
- Some Annual Methotrexate reviews were outstanding

Summary of Audit Findings per GP surgery/practice

GP Practice	Current Methotrexate prescribed			Methotrexate documentation & directions							Folic Acid										Diagnosis				Commenced by			Average Compliance
	Patients on Oral or S/C Methotrexate	Patients records not updated from Methotrexate being stopped	Accuracy of current Methotrexate prescribing on patient medical record	If S/C is it documented in Hospital Only section	Weekly directions state number of tablets & total dose in mg	Tablet strength 2.5mg or 10mg (if 10mg treat as urgent)	Methotrexate directions need amending Y/N (eg MDU)	Weekly directions state day of week methotrexate to be taken (i.e. not just once a week actual day needs to be stated eg Monday)	Methotrexate dose correct as per last hospital letter	Rhematology clinical letter holds accurate information	Folic acid co-prescribed	Folic acid prescribed by Hospital	Folic acid prescribed by GP	Folic acid prescribed by Unclear	If prescribed by hospital is it in the hospital only section	Folic acid directions need amending (eg MDU)	Folic Acid directions state day of week & 'Not to be taken on same day as methotrexate'	Antibiotic co-prescribed	Blood test are up to date	Annual Methotrexate review completed	Rheumatoid Arthritus	Crohn's Disease	Severe Psoriasis (specialist use only)	Other	Rheumatology Department	Dematology Department	Other	
A	23	1	96%	86%	46%	100%	23%	0%	14%	0%	63%	32%	36%	32%	0%	31%	18%	96%	90%	91%	36%	0%	14%	50%	86%	14%	0%	47%
B	25	1	96%	100%	100%	75%	17%	0%	66%	0%	96%	13%	44%	40%	0%	20%	8%	100%	100%	96%	28%	4%	20%	48%	72%	24%	4%	54%
C	8	4	50%	0%	33%	100%	25%	0%	50%	0%	100%	60%	20%	20%	25%	50%	25%	100%	100%	75%	0%	0%	0%	100%	0%	75%	25%	46%
D	25	1	96%	100%	100%	72%	66%	0%	54%	0%	100%	75%	25%	0%	61%	20%	0%	92%	100%	95%	37%	0%	8%	55%	92%	8%	0%	59%
E	47	7	85%	100%	65%	95%	42%	0%	42%	0%	95%	61%	34%	5%	12%	77%	23%	97%	95%	97%	32%	3%	5%	60%	82%	13%	5%	57%
F	51	4	92%	50%	90%	100%	38%	0%	36%	0%	91%	51%	40%	9%	14%	51%	9%	91%	91%	95%	42%	0%	6%	52%	91%	9%	0%	53%
G	46	5	89%	69%	32%	100%	27%	2%	27%	0%	90%	44%	37%	19%	13%	40%	10%	98%	78%	90%	29%	2%	5%	64%	88%	2%	10%	48%
H	64	7	89%	100%	100%	98%	2%	2%	48%	0%	100%	17%	55%	28%	20%	70%	10%	100%	91%	100%	47%	0%	9%	56%	88%	10%	2%	57%
I	65	3	95%	88%	93%	93%	56%	8%	45%	0%	92%	45%	50%	5%	29%	77%	9%	97%	96%	98%	37%	0%	3%	60%	93%	7%	0%	51%
J	20	2	90%	85%	90%	90%	44%	0%	88%	0%	100%	5%	78%	17%	25%	55%	28%	100%	94%	88%	22%	6%	6%	66%	88%	6%	6%	60%
K	57	10	83%	92%	44%	94%	38%	0%	55%	0%	87%	38%	56%	2%	17%	46%	11%	100%	72%	91%	14%	0%	4%	82%	85%	11%	4%	51%
Totals	431	45																										
% Totals	87%			79%	72%	92%	34%	1%	48%	0%	92%	40%	43%	16%	20%	49%	14%	97%	92%	92%	29%	1%	7%	63%	79%	16%	5%	53%
TARGET	100%			100%	100%	100%	100%	100%	100%	100%	100%	N/A	N/A	0%	100%	100%	100%	100%	100%	100%	N/A				N/A			

Recommendations

1. **Clinical Letters:**

   a) Clinical letters must provide all essential prescribing information these are Dose, Form and Frequency and both Methotrexate and Folic Acid.
   b) If the above information is omitted from the letter then a query should be raised to ensure the PMR is accurate
   c) Correct directions must be added and updated as per dose change to a PMR for both Methotrexate and Folic Acid
   d) What is being prescribed and how (oral or subcutaneous) should be clear and mirrored within both PMR and Hospital Section. This includes if a patient discontinues Methotrexate
   e) Who is to supply Folic Acid should be clearly evidence in both the PMR and Hospital Section, as the audit results indicate there is ambiguity as to who supplies Folic Acid, ie, patients are collecting from GP, Hospital, both, or none

2. **Communication**

   To take place regarding out of range levels. Patient should be advised of any raised levels and Consultant review arranged to discuss same

3. **Blood tests**

   To be schedule within review date parameters (guidelines provided in Appendix 4)

4. **Share Care Agreement**

   Implementation of a shared care agreement between Secondary care Consultants and Primary care GPs in order to assure good communication between patients, GPs, hospital Consultants and Pharmacists. Results from this audit show that not all relevant information is currently provided from secondary care providers but more worryingly when it is provided information such as dose and formulation changes are not being updated at primary care level in GP practices from the initial time of commencing methotrexate treatment, sometimes many years previously!

Appendix 1

Suggestions for Drug monitoring in Adults in Primary Care October 2017

High Risk Drug	Monitoring Required	Frequency		Additional Considerations
		First 12 months of commencing treatment	Ongoing treatment	
Methotrexate	FBC	Monthly	Every 3 months	
	U&E	Monthly	Every 3 months	
	LFT	Monthly	Every 3 months	
	CRP (advised by Rheumatology)	Monthly	Every 3 months	
	ESR (advised by Rheumatology)	Monthly	Every 3 months	

Action required if abnormal results

- BSR recommend that treatment be withheld until discussion with consultant specialist if: 1
  - WCC < 3.5 x 109/L
  - Neutrophils< 1.6 x 109/L
  - Unexplained eosinophilia > 0.5x 10 9/L
  - Platelets < 140 x 109/l,
  - AST and/or ALT increase to >100units/ml
  - Unexplained fall in serum albumin <30g/L
  - MCV > 105f/L
  - Creatinine increase > 30% above baseline over 12 months and/or calculated GFR<60ml/min/1.73m2

- Annual flu vaccine should be given, but live vaccines should be avoided.1

- Patients and their carers should be warned to report immediately the onset of any feature of blood disorders (e.g. sore throat, bruising, and mouth ulcers), liver toxicity (e.g. nausea, vomiting, abdominal discomfort and dark urine), and respiratory effects (e.g. shortness of breath).3 12

- Patients should be advised to avoid self-medication with over-the-counter aspirin or ibuprofen. 3

- Patients should be counselled on the dose, treatment booklet, and the use of NSAIDs 3

- The NPSA advise that patients should be instructed to only take their methotrexate once a week on the same day each week and should be issued with a patient-held record card 3,9

References

1. BSR and BHPR non-biologic DMARD guidelines (2017)
2. Current problems in pharmacovigilance. Sept 2003 Vol 29 p 5
3. BNF – accessed via MedicinesComplete (Last updated July 2017)
4. Current Problems in Pharmacovigilence Sept 1997, Vol 23, 12
5. CKS Clinical Topic: DMARDs- methotrexate (last revised July 2015)
6. Best Practice in primary care pathology: review 10. J. Clin. Pathol 2007; 60: 1195-1204
7. NPSA. Methotrexate- patient held blood monitoring and dosage record book
8. BSG Guidelines for the management of inflammatory bowel disease in adults (2011) – Gut 2011, 60(5):571-607
9. NPSA: Improving compliance with oral methotrexate guidelines
10. NICE (2012) Psoriasis: The assessment and management of psoriasis (CG153)
11. NICE public health guidance 43 (2012): Hepatitis B and C: ways to promote and offer testing to people at increased risk of infection
12. 12 NHS England. Never Events List 2015/16. Published Mar 2015 https://www.sps.nhs.uk/wp-content/uploads/2017/12/Drug-monitoring_October-2017.pdf

Resources:

- British National Formulary
- National Institute of Clinical Excellence
- Medicines.org.uk
- Medicines Healthcare Regulatory Authority
- National Rheumatoid Arthritis Society
- British Society for Rheumatology

References

- The National Patient Safety Association (NPSA), (2004) - *Towards the safer use of oral methotrexate,* Accessed 04 May 2020, available from: https://www.sps.nhs.uk/wp-content/uploads/2018/02/2006-NRLS-0102-Towards-safer-umethotrexate-2004-v1.pdf

- West Essex CCG Shared Care Agreement: https://westessexccg.nhs.uk/your-health/medicines-optimisation-and-pharmacy/shared-care-medicines/250-methotrexate-oral-sc-oct-16/file

- Drug Monitoring requirements: https://www.sps.nhs.uk/wp-content/uploads/2017/12/Drug-monitoring_October-2017.pdf

Audit Log

Attached under separate document