SAFER®
SAFER USE OF HIGH RISK MEDICINES

Waitemata District Health Board
Best Care for Everyone

ISOTRETINOIN - SAFE PRESCRIBING - HIT THE SPOT!

- INFORM PATIENTS THAT ISOTRETINOIN IS A POTENT TERATOGEN
- USE ONLY WHERE CLEARLY INDICATED
- PRESCRIBE THE LOWEST EFFECTIVE DOSE
- ADVISE PATIENTS ABOUT THE POTENTIAL FOR ADVERSE REACTIONS
- PERFORM A THOROUGH CONSULTATION AT EACH VISIT
- ARRANGE ON-GOING MONITORING

Isotretinoin is indicated for patients with severe forms of nodulocystic acne that are resistant to other therapy.[1,2] Isotretinoin is a medicine that adolescents may be aware of, and prescribers may experience pressure to prescribe it.[3] Inform patients about the potential harm that may arise from isotretinoin use, especially the teratogenic effects.

INFORM PATIENTS THAT ISOTRETINOIN IS A POTENT TERATOGEN

Isotretinoin is classified as Pregnancy Category X; it is a potent teratogen and can cause severe foetal malformations.[4] There is an extremely high risk that a deformed infant will result if pregnancy occurs while taking isotretinoin in any amount, even for short periods. Reported malformations include:[1]

- effects on the central nervous system (hydrocephalus, microcephalus)
- cardiovascular abnormalities
- facial dysmorphia
- absence or deformity of ears
- thymus and parathyroid gland abnormalities

A large US study followed 151 births in women who were exposed to isotretinoin during pregnancy; 47% of these women had children with congenital malformations.[5] Two cases of congenital abnormalities associated with isotretinoin use have been reported to CARM in New Zealand.[4]

Note: Inform patients that they need to continue with contraception at least 1 month after stopping isotretinoin.[1]

Men taking isotretinoin

No contraceptive precautions are required for males who are taking isotretinoin; birth defects have not been identified in children fathered by men who have taken isotretinoin.[1]

USE ONLY WHERE CLEARLY INDICATED

Isotretinoin should only be considered if the patient has already trialled other available treatments and received an inadequate response. Isotretinoin is contraindicated in:[1]

- women who are pregnant or who may become pregnant
- women who are breastfeeding
- hepatic insufficiency
- hypervitaminosis A
- severe hyperlipidaemia

Clinically significant serum triglyceride elevations should be controlled before starting isotretinoin and during treatment to reduce the risk of acute pancreatitis.[1]

Patients with severe renal insufficiency should start on a lower dose (10mg per day); the dose can be then adjusted according to tolerability.[1,2]

Note: Inform patients that blood donation is contraindicated during isotretinoin treatment, and for at least 4 weeks following discontinuation.[2]

PRESCRIBE THE LOWEST EFFECTIVE DOSE

Recent evidence suggests that isotretinoin is best prescribed using a lower daily dose, (eg 10-20mg daily). Lower doses appear to be as effective as higher doses, and are associated with fewer adverse effects.[6] Isotretinoin is best taken with food to aid absorption.

A suggested regimen is to initiate isotretinoin at 10-20mg daily and to continue until all acne lesions have resolved (usually between 3-5 months), and then to reduce the dose to 5-10mg daily for a further 2-4 months to avoid relapse and scarring.[6]

Note: The 5mg capsule is not currently subsidised; consider prescribing 10mg on alternate days instead.

➥ continued

ISOTRETINOIN

ADVISE PATIENTS ABOUT THE POTENTIAL FOR ADVERSE REACTIONS

A range of troublesome adverse effects can occur with isotretinoin use, these are generally dose-related.[1] Examples include:[7]

- transient flare-up of acne
- inflammation and dryness of the lips
- dry eyes (causing difficulty with contact lens use)
- dry nasal mucosa (and nose bleeds)
- dry skin and photosensitivity
- headaches
- muscle aches (and reduced vigorous exercise tolerance)
- fatigue
- visual disturbances (including night blindness)
- thinning of scalp hair and reversible hair loss
- hyperostosis and bone changes

Some of these reactions can be relieved with simple interventions, eg using emollients for dry skin.[7] Advise patients to protect their skin from direct sunlight and to avoid sunbeds.[2] Patient resources are available via www.dermnetnz.org and www.saferx.co.nz, and in the BPAC acne prescribing tool.

Rarely, isotretinoin may cause a transient and reversible rise in liver transaminases. Often these changes have been within the normal range and values have returned to baseline while on treatment. If transaminase levels do exceed normal values, a dose reduction or cessation of isotretinoin may be necessary.[1]

Serum triglyceride concentrations may also rise during isotretinoin therapy. These changes are reversible with a dose reduction or discontinuation of treatment; sometimes these increases may respond to dietary measures.[1]

Isolated cases of benign intracranial hypertension have been reported with isotretinoin, and with tetracyclines. For this reason, supplementary treatment with tetracyclines is contraindicated.[1]

Psychiatric side-effects

Mood changes, depression, and suicidal ideation (including suicide attempts) have been reported in patients who are taking isotretinoin.[5] Assess patients for signs of depression and suicidal thoughts before starting isotretinoin therapy.[8]

Note: A direct causal link between isotretinoin use and depression or suicide has not been clearly established, and studies of mood change have found that mood and wellbeing usually improve as acne improves.[8]

PERFORM A THOROUGH CONSULTATION AT EACH VISIT

Extended consultations are required to ensure isotretinoin is used safely. Adequate time is needed to fully discuss the risks and benefits of isotretinoin therapy.

Pregnancy

Although the risks of foetal damage are well known, there are still reports of pregnancies occurring in women who have taken isotretinoin.[4]

Thorough consultations with intensive counselling are essential when prescribing isotretinoin to women of childbearing age.[1,4] Each woman should understand the implications of pregnancy, and must be able to comply with the requirements for adequate contraception.

Special Authority criteria requires that if the patient is female: '*The patient has been counselled and understands the risk of teratogenicity if isotretinoin is used during pregnancy, and the applicant has ensured that the possibility of pregnancy has been excluded prior to the commencement of the treatment and that the patient is informed that she must not become pregnant during treatment and for a period of 1 month after the completion of treatment.*'[9]

Medsafe recommends the following approach when prescribing isotretinoin to ALL women of childbearing potential, including those who do not usually use contraception because of infertility:[4]

- take a current sexual history
- take a menstrual history
- arrange a pregnancy test
- provide contraceptive advice
- prescribe contraceptives
- ensure the patient understands the risks
- advise to start taking isotretinoin during their next period
- arrange regular pregnancy tests
- continue with contraception for one month after stopping

Women must practice effective contraception for at least 1 month before starting treatment, during treatment, and for 1 month after stopping treatment. Oral progestogen-only contraceptives are not considered effective, and barrier methods should not be used alone.[2]

Additional advice may be found in the data sheet[1] and the Medsafe prescriber update.[4]

➥ continued

ISOTRETINOIN

Depression

All patients need to be informed about the risk of depression before isotretinoin begins, and be monitored for the development of depression during treatment. It is important that patients (and their families), are provided with information about depression and suicidal ideation.[5] Patients should be advised to report symptoms promptly so they can be they can receive appropriate psychiatric support.[1,5]

Inflammatory bowel disease (IBD)

Isotretinoin has been associated with IBD; patients should be advised to discontinue isotretinoin if they experience severe diarrhoea.[1]

Cosmetic treatments

Patients are advised to avoid **aggressive dermabrasion** and **wax epilation** during treatment and for 6 months after stopping isotretinoin due to a risk of scarring and dermatitis.[1]

ARRANGE APPROPRIATE ON-GOING MONITORING

Patients taking isotretinoin should understand the need for rigorous follow-up, preferably on a monthly basis.[1] Prescribers should consider giving patients prescriptions that only supply **1 month** of isotretinoin at a time to facilitate regular patient review.

Blood testing[1]

Test required	Before therapy	After one month	During treatment	After treatment
Pregnancy	Yes	Yes	Monthly	1 month after stopping
Serum lipids	Yes	Yes	-	At end of treament
Liver function	Yes	Yes	Every 3 months	-

Depression

ALL patients should be reviewed for signs of depression at each visit. If patients present with depression, isotretinoin should be discontinued[2,10] and a psychiatric or other mental health review arranged, as necessary.[1]

Note: Symptoms of depression and suicidal thoughts may not resolve simply by stopping treatment with isotretinoin; continue to assess and monitor these patients.[8]

Best Practice Decision Support

Special Authority criteria[9] for isotretinoin recommends that a computer-based decision support tool is used when prescribing. 'Bestpractice Decision Support' is a web-based system that helps to support general practice in the management of patient screening, risk assessment, management and referral.

Of the modules that are available free of charge to New Zealand health professionals, there is a module for 'acne' which includes 'isotretinoin'.

The acne module helps with the assessment of acne, provides access to resources and describes treatment options. The isotretinoin section has information about patient consent, monitoring and prescribing, including quick access to the Special Authority process. Patient information is also available.

ACKNOWLEDGEMENTS

We wish to thank Blair Wood, Consultant Dermatologist, Waitemata District Health Board, for his valuable contribution to this bulletin.

REFERENCES

1. H Douglas Pharmaceuticals Ltd Datasheet Oratane. www.medsafe.govt.nz/profs/datasheet/o/oratanecap.pdf (Accessed 14-07-14)
2. New Zealand Formulary. Isotretinoin http://nzf.org.nz/nzf_6452.html (Accessed 14-07-14)
3. PHARMAC. Changes to prescriber restrictions for acitretin and isotretinoin. 19 Dec 2008. Available on www.pharmac.govt.nz (Accessed 15-07-14)
4. Rademaker M. Avoiding Teratogenicity with Isotretinoin. Prescriber Update 2002;23(3):35-6 www.medsafe.govt.nz/profs/Puarticles/teratogen.htm (Accessed 14-07-14)
5. Medsafe Publications. Acne, isotretinoin and depression – inform and monitor. Prescriber Update 2011;32(3):25-6 www.medsafe.govt.nz/profs/PUArticles/IsotretinoinSept2011.htm (Accessed 14-07-14)
6. Oakley A. Prescribing update: Low dose isotretinoin for acne? Best Practice Journal 2013;56:16-17 www.bpac.org.nz/BPJ/2013/November/docs/BPJ56-acne.pdf (Accessed 14-07-14)
7. DermNet NZ. Isotretinoin. http://dermnetnz.org/treatments/isotretinoin.html (Accessed 15-07-14)
8. NPS Medicine Wise. Isotretinoin under the spotlight again. Health News and Evidence; 25-07-14; www.nps.org.au/health-professionals/health-news-evidence/2014/isotretinoin-suicide (Accessed 01-08-14)
9. Pharmac. Special Authority Isotretinoin SA1475 December 2014. www.pharmac.govt.nz/2014/12/01/SA1475.pdf (Accessed 15-12-14)
10. Rademaker M. Acute depression and isotretinoin. Medsafe Prescriber Update 1998;17:17-19 www.medsafe.govt.nz/profs/PUarticles/isotretinoin.htm (Accessed 14-07-14)

No: 0182-01-022, Issued Jan 2015; Review Jan 2018